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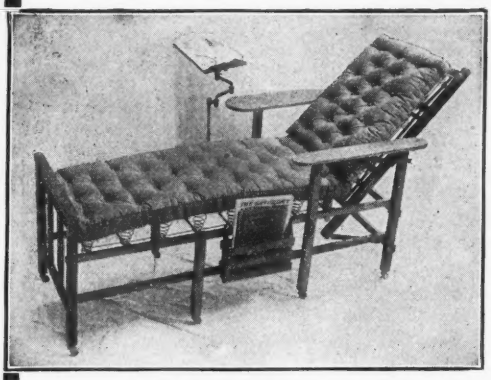

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ATTEMPTS TO REDUCE THE RESISTANCE OF THE GUINEA PIG TO TUBERCULOSIS BY MEANS OF VARIOUS AGENTS

THE EFFECTS OF THE ROENTGEN RAY, BENZENE, THORIUM X, TUBERCULIN, ETHER AND CHLOROFORM

H. J. CORPER

From the Laboratories of the City of Chicago Municipal Tuberculosis Sanitarium

Murphy and Ellis (1), on the basis of experiments reported by Lewis and Margot (2), who noted that rats and mice experimentally infected with tuberculosis developed large spleens and that those splenectomized lived longer after inoculation than normal animals, believed they saw a relationship between the lymphocyte and resistance to tuberculosis. They tested their ideas by infecting mice with bovine tubercle bacilli (1 mgm.) and, using as a criterion the duration of life, the X-rayed mice usually died in about one-third (7 and 9.7 days as compared to 18.5 and 23.3 days) the time required for the controls. As a result of their experiments they conclude, "Mice, either normal or splenectomized, after exposure to X-ray are markedly more susceptible to bovine tuberculosis than are normal animals." Morton (3) receiving his cue from this work applied the X-ray to hastening the guinea pig diagnosis for human tuberculosis. He found one massive exposure to the X-ray to reduce the total leucocytes from 12,000 to 15,000 cells per cubic millimeter by over one-half (4000 to 6000), the reduction being mainly one of lymphocytes. The animals were radiated ten minutes with the Coolidge tube, the target being 12 inches from the base of the box containing the guinea pig. A 5 milliampere current was passed through the tube, backing up $8\frac{1}{2}$ inches of spark between points. Urine from ten cases of tuberculosis of the genito-urinary tract was used for infecting the guinea pigs and from this work Morton concludes that, "In renal tuberculosis when it is necessary to resort to the use of animals, it ordinarily requires from five to seven weeks, while by the use of X-rayed guinea pigs the diagnosis can be made in from eight to ten days. The resistance can be sufficiently lowered by one massive dose of X-ray administered either shortly before or after the inoculation of the material to be tested."

There are a number of substances which act similarly (differing only in minor details) to the X-ray upon the animal economy, notably, benzene and thorium X (or other radioactive materials), and the investigations to be reported in this paper were carried on with a view to finding a substitute for the roentgen ray, for not every one possesses an X-ray machine or has access to one, and we hoped to make it possible for any physician to reduce the time for making a diagnosis of tuberculosis by the use of the guinea pig.

Heineke (4) and others have shown that in proper doses the X-ray has a direct and destructive action on the lymphoid and myeloid tissues. Hektoen (5) found that the formation of lysin may be restrained thereby to a marked degree in white rats while Simonds and Jones (6) observed that X-rayed rabbits revealed an appreciably lowered formation of agglutinins, although not so marked as in those injected with benzene. The formation of bacteriolysins for B. typhosus was not greatly interfered with, while the opsonic content and complement fixing power of the serum and of the X-rayed rabbits did not differ greatly from that of control animals. Heinrich (7) noted that guinea pigs X-rayed immediately after sensitization revealed a marked reduction in sensibilin (did not react as violently anaphylactically). The leucotoxic action of benzene in cases of leukemia and in normal individuals has been reported any number of times. Wachtel (8) obtained a drop from 102,000 to 37,000 leucocytes, Barker and Gibbes (9) from 191,000 to normal, etc., (10). Selling (11) found that in rabbits benzene in suitable dose causes profound destruction in the hemopoetic structures, especially of the marrow. Bianchi (12) obtained an almost complete disappearance of blood platelets after benzene injections while Weiskotten, Schwartz and Steensland (13) noted a rapid decrease in the peripheral circulating leucocytes. Simonds and Jones (14) noted a depression in the production of hemolysins, agglutinins, and opsonins in rabbits injected with benzene, while Hektoen (15) obtained a greatly reduced production of specific precipitin and lysin in rabbits and white rats. The leucocytes of the benzene rabbits were also of reduced phagocytic power. Schiff (16) found that large doses of benzene reduced the anaphylactic reaction of sensitized guinea pigs. White and Gammon (17) gave rabbits benzene by inhalation after inoculation with tubercle bacilli and believed that the benzene rabbits were less resistant to tuberculosis than the untreated.

Thorium X, one of the radioactive substances, easily soluble in physiological salt solution, possesses decided advantages over the X-ray for experimental use in that it can be injected, its only drawback being that the solution on standing loses strength but in a definite curve form so that its strength on subsequent days can be approximately figured. Plesch and Karczag (18), found that the bones and bone marrow in rabbits fixed 38 per cent of the thorium X in one hour, and 64 per cent after twenty-four hours; while Pappenheim and Plesch (19) noted cell degeneration, especially in the bone marrow, liver and kidney. Arneth (20) observed a marked drop in the total leucocytes (with a relative increase in the lymphocytes) in rabbits given thorium X. Rosenow (21) obtained a decrease of the total leucocyte count, the lymphocytes being at first chiefly concerned. Later the relation between the lymphocytes and polymorphonuclear leucocytes changes completely and the latter may be made to disappear entirely while all the remaining white corpuscles are lymphocytes. No observations on the effect of thorium X upon antibodies was found in the literature but experiments being carried out by Dr. Hektoen and the author have revealed a great reduction of precipitin and in some cases of the lysin for sheep blood.

Since guinea pigs were used throughout this investigation and there seems to be some question of a gauge to indicate whether or not a certain substance has a favorable or detrimental influence upon the tuberculosis in the animal, it might be stated that the macroscopic anatomical involvement was used as such a criterion. Death of the animal as was observed by Marmorek (22) is of minor significance and Krause (23) points out the importance of accident in determining the issue.

Benzene being easily obtained on the market and administered to animals was initially chosen as the most suitable substitute for roentgen raying to increase the susceptibility of the guinea-pig to tuberculosis. The main drawback to its use by injection, which for this purpose seemed most suitable, was the necroses and ulcers resulting at the site of such injections if the commonly used mixture of one part of benzene[1]

[1] In the early experiments carried on with benzene the futility of obtaining a pure benzene on the American market was realized, all the preparations obtained (even those labelled thiophene free) being highly toxic and containing considerable amounts of thiophene. Preparations from Merck and C. A. F. Kahlbaum did not prove to be better in this respect. Preparations of benzene from benzoic acid which were much more expensive, however, contained no thiophene and gave the gauge by which was judged the purity of preparations finally obtained from the coal tar benzene. The benzene was purified by allowing it to stand over concentrated sulphuric acid, c. p., for several days, with frequent shaking and changing the

and one part of olive oil was used. This destructive local effect of the benzene-olive oil mixture when given subcutaneously also made the dosage an uncertain factor since part of the benzene may remain in the necrotic slough. With a view to obtaining a better vehicle for the benzene, especially one that would not be so injurious at the site of injection, preliminary experiments were performed as indicated below.

LOCAL TOXICITY OF BENZENE MIXTURES

The following mixtures were tested for local toxicity, according to a method previously described (24), by the intracutaneous injection of 0.1 to 0.2 cc. into the skin of the abdomen of a guinea pig:

1. One part olive oil and one part benzene (liquid at room temperature).
2. One part cotton seed oil and one part benzene (liquid at room temperature).
3. One part liquid petrolatum and one part benzene (liquid at room temperature).
4. One part paraffine (m.p. 40°C.) and one part benzene (liquid at room temperature).
5. Two parts paraffine (m.p. 40°C.) and one part benzene (just liquid at 40°C.).
6. Three parts paraffine (m.p. 40°C.) and one part benzene (semisolid at 40°C.).
7. One part paraffine (m.p. 56°C.) and one part benzene (solid at room temperature and just liquid at 40°C.).
8. One part vaseline (ordinary) and one part benzene (solid at room temperature and liquid at 40°C.).
9. One part vaseline (ordinary) and two parts benzene (semisolid at room temperature and liquid at 40°C.).

Daily observations of the site of injection were made with the following brief findings: Mixtures 1, 2, 3, 4, and 9 produced a local necrosis on the first day which persisted and discharged in about a week; 5 and 6 produced erythema on the first and second days, and necrosis was visible only after the third day; 7 and 8 never brought about necro-

acid until no more brown or yellow color was imparted to it. The supernatant benzene was then poured off and treated with a weak solution of sodium hydroxide until slightly alkaline to phenolphthalein. The pure benzene was then distilled off at about 80°C. This preparation proved to be equal in toxicity tests to that of the benzene prepared from benzoic acid.

sis but on the ninth day 7 produced a small hard lump and 8 set up a slight induration at the site of injection.

The choice of the above mixtures to avoid the local destructive action of the benzene would seem to be one part of ordinary vaseline and one part of benzene, or one part of paraffine (m.p. 56°C.) and one part of benzene. The paraffine mixture was arbitrarily chosen for experimental use because the paraffine was a more constant and a purer material.

In order to determine the lethal dose of the mixture of equal parts of paraffine (m.p. 56°C.) and benzene, a series of full grown male white rats (about 250 grams) were injected subcutaneously with varying amounts of this mixture, and briefly it was found that they would tolerate 10 cc. (that is 5 cc. benzene) while 15 cc. of the mixture (7.5 cc. benzene) usually caused death in one or two days. Guinea pigs in proportion tolerated about the same amounts.

ABSORPTION OF BENZENE FROM PARAFFINE (M.P. 56°C.) MIXTURE

The ideal method of administering the benzene would naturally be in a form in which one injection would suffice and from which a slow absorption would still take place extending over a long period of time. The paraffine (m.p. 56°C.) benzene mixture seemed to fulfill this requirement. In order to determine, therefore, the rate of absorption of the benzene by the tissues, after injection in this form, a series of guinea pigs were each given subcutaneous injections of from 10 to 20 cc. of the mixture, and as much as possible of the local paraffine mass and adherent tissues was removed at regular intervals and analyzed for benzene and paraffine content. The method of analysis was only approximate (giving figures only within 5 to 10 per cent) and briefly was as follows: The tissue was thoroughly extracted with hot ether in a Greene extraction apparatus and from this the ether was entirely distilled off and then the benzene fraction distilling between 79° and 81°C. was collected and measured. The residue remaining after distillation was saponified with an excess of 5 per cent sodium alcoholate to remove the ordinary fats, and while hot was poured into a graduated cylinder containing hot distilled water. In this water all soaps, glycerol, etc., would dissolve while the paraffine floated to the top, whence it was drawn off by means of a warm pipette and run into a 15 cc. graduated centrifuge tube for final washing with distilled water and measuring. The results of these analyses are indicated in table 1.

The results of the above experiment indicate that benzene is absorbed in the guinea pig from the mixture of equal parts of paraffine (mp. 56°C.) and benzene when injected subcutaneously, about two-thirds disappearing by the second day, after which absorption is slow, being completed in about twenty days.

TABLE 1

Absorption of benzene from mixture of equal parts of paraffine (m.p. 56°C.) and benzene

INTERVAL BETWEEN INJECTION AND REMOVAL FOR ANALYSIS	TOTAL VOLUME BENZENE	TOTAL VOLUME PARAFFINE	PERCENTAGE BENZENE TO PARAFFINE
days	*cc.*	*cc.*	
0	4.0	4.4	91
0	2.2	2.5	88
1	1.8	3.5	51
2	1.4	4.2	33
3	0.9	4.6	20
5*	1.5	9.0	16
10	0.6	4.6	13
20*	Trace	4.1	

* The 5-day guinea pig received 19 cc. and the 20-day, 20 cc., of the mixture while all the other animals had received 10 cc. subcutaneously.

EFFECT OF THE INJECTION OF BENZENE UPON TUBERCULOSIS IN THE GUINEA PIG

A series of ten male guinea pigs, all about equal in weight (400 to 600 grams) were given a subcutaneous injection in the left lower quadrant of the abdomen of 0.001 mgm. human tubercle bacilli (no. 2690), and on the same day 15 cc. of a mixture of equal parts of benzene (absolutely thiophene free) and paraffine (m.p. 56°C.) was injected subcutaneously into the right lower quadrant of the abdomen of 5 of them, while the other 5 were used as normal controls. The animals were kept under close observation, especially the local glands, and were sectioned at thirty-nine, fifty-six and seventy days with the results recorded in table 2.

The above experiment was repeated, but, instead of giving a single large injection of benzene, smaller injections of 2 to 3 cc. were given on alternate days, totalling 10 injections. This series included 12 male guinea pigs about 400 to 600 grams in weight that were given 0.0003 mgm. of culture no. 2690 human tubercle bacilli on the same day that the benzene injections were initiated (and continued) in 7 of them, the remaining 5 serving as controls. The results are given in table 3.

From these experiments it is to be noted that neither a single large subcutaneous injection (7.5 cc.) of benzene, or repeated small (1 to 1.5 cc. on alternate days for twenty days) injections have any influence upon the course of macroscopic anatomic tuberculosis in the guinea pig infected with human tubercle bacilli.

TABLE 2

Effect of a single large subcutaneous injection of benzene upon tuberculosis in the guinea pig

DAYS	CONTROLS	BENZENE TREATED
39	+*	+
56	++ ++	++ +++
70	+++ ++++	+++ +++

* Throughout this paper the following markings will indicate the amount of anatomical tuberculosis found in the guinea pigs on sectioning:

− No macroscopic anatomic tuberculosis.

+ Distinctly enlarged local and slightly enlarged retroperitoneal glands.

++ Enlarged local and retroperitoneal glands and slight involvement of the spleen.

+++ Enlarged local and retroperitoneal glands, spleen markedly involved, the peritracheal glands enlarged and the lungs slightly involved.

++++ Massive involvement of all the glands, spleen, lungs and liver.

TABLE 3

Effect of repeated injections on alternate days of benzene in paraffine upon tuberculosis in the guinea pig

DAYS	CONTROLS	BENZENE TREATED
6		−*
17	+	+*
22	+	+*
		+
35	++	++*
65	+++ +++	+++ ++++

* The asterisk indicates that the guinea pig died, its absence that the animal was killed for sectioning.

EFFECT OF BENZENE INHALATION UPON TUBERCULOSIS IN THE GUINEA PIG

Benzene lends itself well for inhalation experiments, and believing that thus a more profound effect of the benzene could be obtained the following experiments were performed: A series of 12 guinea pigs were

given a subcutaneous injection into the lower left quadrant of the abdomen of 0.0003 mgm. of culture no. 3239 human tubercle bacilli, and commencing on the same day 8 of the guinea pigs were given inhalations of benzene vapor mixed with air once or twice daily. An ordinary glass walled box was prepared for this purpose. They were sectioned at various intervals as indicated in table 4.

TABLE 4

Effect of benzene inhalation (initiated at time of infection) upon tuberculosis in the guinea pig

DAYS	CONTROLS	BENZENE TREATED
5		−*
15		+*
21	+	+
31		+
40	+++	++
56	++	++
72	+++	+++ ++++

* This guinea pig died.

The above experiment was repeated but the 5 benzene treated guinea pigs were given inhalations for twelve days before infection with 0.0003 mgm. of culture no. 3135 human tubercle bacilli and they were continued for twenty days after infection. The results are given in table 5.

TABLE 5

Effect of benzene inhalations (initiated twelve days before infection and continued) upon tuberculosis in the guinea pig

DAYS	CONTROLS	BENZENE TREATED
24	++	++
		++
43	+++	+++
		+++
58	++++	++++

The above experiments indicate that benzene administered to guinea pigs by inhalation to the point of unconsciousness daily during a period of about a month, beginning inhalations at the time of infection or twelve days prior, has no influence upon the course of tuberculosis as measured by the macroscopic anatomic involvement.

EFFECT OF ROENTGEN RAY UPON TUBERCULOSIS IN THE GUINEA PIG

Having failed to reduce the resistance of the guinea pig to tuberculosis by means of benzene it was deemed advisable to repeat the investigations with the roentgen ray, but in animals given definite amounts of human tubercle bacilli and suitably controlled.

Since Morton was able to reduce the time necessary for the development of tuberculosis in guinea pigs for diagnostic purposes to about ten days by means of a single large exposure to the X-ray, a series of 10 guinea pigs (5 treated and 5 controls) was used to test the effect of a single large exposure to X-ray upon the macroscopic anatomic tuberculosis found in these animals at various times. The exposure given the day of infection consisted of raying each pig in a box for ten minutes using a Coolidge tube through which was passed a 5 milliampere current backing

TABLE 6

Effect of a single large exposure (Morton's method) to the roentgen ray upon tuberculosis in the guinea pig

DAYS	CONTROLS	EXPOSED
4		
12	−	−*
22	+	−*
31	++	+
48	+++	++
	+++	+++

* An asterisk indicates that the guinea pig died.

up 8½ inches of spark, the target being about 12 inches from the base of the box containing the guinea pig. The guinea pigs were infected by injecting subcutaneously into the left lower quadrant of the abdomen 0.000,001 mgm. of culture no. 1687 human tubercle bacilli. The results obtained are given in table 6.

The above experiment was repeated but the guinea pigs were given a single large exposure to X-ray (5 milliampere, 9 inch spark gap, for ten minutes, target to base of box being 12 inches) followed by about eight smaller exposures (for five minutes, 6 inch spark gap and 3 to 4 milliamperes) and the total leucocytes were counted on alternate days throughout the entire experimental period (for obvious reasons only the lowest count is given in the table).

In this experiment was included 5 treated guinea pigs and 3 controls, all infected on the day of the large exposure to the X-ray by the subcutaneous injection of 0.000,001 mgm. of culture no. 1687 human tubercle bacilli. The findings and lowest leucocyte counts of the exposed guinea pigs are given in table 7.

The above experiments were repeated using another culture, no. 3317, of virulent human tubercle bacilli (0.000,000, 3 mgm. being injected into each guinea pig) with almost identical results.

In order to further test whether it was at all possible to influence the tuberculosis in the guinea pig by means of roentgen ray exposures, a series of 6 male pigs (about 400 to 600 grams in weight) were X-rayed (ten minutes, $9\frac{1}{2}$ inch spark, 5 milliamperes) daily or on alternate days

TABLE 7

Effect of a single large and subsequent smaller exposures to the roentgen ray upon tuberculosis in the guinea pig

DAYS	CONTROLS	EXPOSED	
		Results	Lowest leucocyte count
17		−	2,300(7)**
21		−*	1,950(7)
27	+	+	2,655(9)
29	++ ++	+ +	2,750(12) 2,550(14)

* This guinea pig died on the twenty-first day.

** The figure after the total leucocyte count indicates the day on which such count was obtained.

as was necessary to keep the leucocytes at a low level. The leucocyte counts were used as a gauge, being reduced to about 2500 before infection. Infection was performed by the subcutaneous injection of 0.000,000,5 mgm. of culture no. 1687 virulent human tubercle bacilli and as nearly as possible the leucocyte count was kept down to 2500 per cmm. throughout the twenty-eight days of experimentation. Only the average leucocyte count for the entire period and the results of this experiment are given in table 8.

The above experiments indicate that a single large exposure to the roentgen ray (Morton's method) or a single large one, followed by a series of smaller exposures, has no influence upon the progress of the macroscopic anatomic tuberculosis in the guinea pig, even though this produces a temporary leucopenia (as low as 2000 leucocytes per cubic

millimeter of blood). A leucopenia (averaging as low as approximately 2500 leucocytes per cubic millimeter of blood) produced by the roentgen ray and existing throughout the entire period of infection with virulent human tubercle bacilli has just as little influence upon the macroscopic anatomic tuberculosis in the guinea pig.

TABLE 8

Effect of continued low leucocyte level produced by means of the roentgen ray upon tuberculosis in the guinea pig

DAYS	CONTROLS		EXPOSED	
	Results	Average leucocytes	Results	Average leucocytes
28	++	13,750	+	2,750
	+	12,500	+	2,500
	++	11,500	+	2,250
			+	3,000
			+	2,750
			++	2,250

EFFECT OF THORIUM X UPON TUBERCULOSIS IN THE GUINEA PIG

Thorium X lends itself much more readily to reducing the circulating leucocytes than the roentgen ray, but at present cannot be bought on the market.[2] Since accurate measurements of the thorium X were not necessary a simple and rapid approximate method was used throughout these experiments. It consisted briefly of determining the rate of complete discharge of an electroscope made from an ordinary small square tin can with lid, through the top of which was suspended a wire attached to a narrow copper plate to which was attached a thin leaf of aluminum, the wire (sealed in by sulphur) and leaf support being insulated from the tin can by means of a piece of briar pipe stem. In the bottom of the can a small hole was perforated and under this was placed the thorium X in a small metal pill box cover, mixed with kaolin and dried. The leaf charged by means of an ebonite rod, should not appreciably drop within two minutes in control tests. The thorium X was then placed under the electroscope (starting with a low concentration) having been prepared in various dilutions and allowed to remain for two minutes

[2] The thorium X used in these experiments was prepared from a supply of radio thorium kindly contributed for this work by Professor Herbert N. McCoy of the Department of Chemistry of the University of Chicago and the Carnotite Reduction Company, Professor G. L. Wendt assisting in the preparation.

before a reading was made. The amount of thorium X necessary to cause a complete drop of the aluminum leaf in one minute (on three successive readings) was taken as the arbitrary unit used in toxicity experiments. The solutions gradually lose their strength, but after one reading has been obtained the amount of active material remaining for several days can easily be computed. The thorium X was prepared from the radiothorium (in dilute hydrochloric acid) by passing ammonia gas through the solution until just alkaline to litmus, and filtering off the flocculent precipitate (which is again dissolved in a small amount of hydrochloric acid and can be extracted anew, thus giving almost as much thorium X as previously and this process can be repeated for several years at weekly intervals). The filtrate is evaporated to dryness and the ammonium chloride completely driven off in an evaporating

TABLE 9

Toxicity of thorium X for guinea pigs

DOSE INTRAPERITONEALLY (ARBITRARY UNITS)*	DAYS OF DEATH	LOWEST LEUCOCYTE COUNT OBTAINED	DAY OBTAINED
1000	6		
500	7	500	5
250	10	275	9
100	15	425	13
50		1625	6
10		2150	9

* A unit is only approximate and is the amount of thorium X necessary to cause a complete discharge of the electroscope used within one minute time.

dish over the free flame, when the thorium X remains. This can be dissolved in sterile physiological salt solution and is ready for injection either intravenously, intraperitoneally, or subcutaneously after testing its strength.

In a combined experiment the effect of the intraperitoneal injection of a single large dose (50 units) of thorium X and repeated small doses (4 to 6 injections of 10 to 15 units) was tried upon male guinea pigs (about 400 to 600 grams in weight) infected by the subcutaneous injection of 0.000,000,1 mgm. of culture no. 1687 virulent human tubercle bacilli on the day the thorium X injections were initiated. The results of the experiment are given in table 10.

In order to reveal the maximum effect obtainable by means of thorium X a series of male guinea pigs was treated until the leucocytes were

at a low level and then were infected, using 0.000,001 mgm. of culture no. 1687 virulent human tubercle bacilli injected subcutaneously. The leucocytes were maintained at a low level throughout the entire experimental period by means of repeated injections of thorium X as indicated necessary by the leucocyte counts. The results of the experiment are given in table 11.

TABLE 10

Effect of a single large or repeated small injections of thorium X upon tuberculosis in the guinea pig

DAYS	CONTROLS	LARGE INJECTION	REPEATED SMALL INJECTIONS
11		−(1025)*	−(975)*
24	++(13175)**		++(1125)* +(500)
34	++(16800) +(13250) ++(14250)	+(3125) +(1450)	++(1750) +(1250)

* The single asterisk indicates the animal died.

** The figure given after the tuberculous involvement indicates the lowest leucocyte count obtained throughout the experimental period.

TABLE 11

Effect of a continued low leucocyte level produced by means of thorium X upon tuberculosis in the guinea pig

CONTROLS*		THORIUM X TREATED	
Results	Average leucocyte count	Results	Average leucocyte count
+	11,250	++	2,500
++	10,000	+	1,150
++	12,750	+	1,750
+	13,500	++	1,675
		+	1,050
		+	1,675

* All the guinea pigs were killed twenty-five days after infection.

The experiments with thorium X in a way corroborated the findings with the roentgen ray in that a single large injection of thorium X sufficient to temporarily reduce the total circulating leucocytes to a low level (about 1500 per cubic millimeter), or repeated small injections, had no influence upon the progress of tuberculosis produced by virulent human tubercle bacilli in guinea pigs. Likewise a leucopenia (averaging as low as 1000 leucocytes per cubic millimeter) produced by thorium

X and maintained throughout the entire period of infection had just as little effect upon the progress of the tuberculosis.

Six rabbits were infected by the intravenous injection of 0.1 mgm. of virulent human tubercle bacilli after the leucocytes had been reduced by means of thorium X in 3 of them and maintained low (about 1500 to 2500 per cubic millimeter) for the entire period of infection of one month; the other 3 rabbits serving as controls. No appreciable difference was noted on section (within the limits of variation normally found) between the control rabbits and those in which the circulating leucocytes were maintained at a low level by means of thorium X.

EFFECT OF TUBERCULIN (KOCH'S O. T.), ETHER, AND CHLOROFORM UPON TUBERCULOSIS IN THE GUINEA PIG

A few other substances of minor importance, however, were also tried in an effort to increase the susceptibility of the guinea pig to tuberculosis.

The tuberculin (Koch's O. T.) used in the following experiment[3] was an American preparation which, however, compared well with a German preparation of Koch's O. T. and Tuberculin A. F. (Farbwerke Meister, Lucius and Brüning), labelled officially tested, in that normal and tuberculous (with well marked systemic involvement) guinea pigs tolerated 2 cc. given intraperitoneally once, or repeated injections of 1 cc. daily (totaling 7 cc.).

The tuberculin was given to one set of guinea pigs in large doses, that is, 1 cc. diluted with 4 cc. sterile 0.9 per cent salt solution, intraperitoneally daily for five days, and then on alternate days 5 more injections and in small doses, that is, 0.2 cc. tuberculin daily for twenty days, injections being initiated on the day of infection with 0.000,000,01 mgm. virulent human tubercle bacilli, (culture no. 1687), given subcutaneously. The results are given in table 12.

Tuberculin (Koch's O. T.) obtainable on the market (either in large doses of 1 cc. daily for five days and on alternate days totalling 10 cc., or in small doses 0.2 cc. daily for twenty days) had no appreciable influence upon the macroscopic anatomic tuberculosis in guinea pigs produced by virulent human tubercle bacilli.

[3] The tuberculin used was kindly contributed for investigative work by Dr. E. King of Parke, Davis & Co., Detroit, Mich.

The ether inhalations, mixed with air, were given to the guinea pigs in a box especially constructed for the purpose. In the first experiment (table 13 a) inhalations were given daily to the point of anaesthesia once a day for about fifteen days and since the ether treated guinea pigs seemed to reveal slightly less tuberculosis than in the controls the

TABLE 12

*Effect of tuberculin (Koch's O.T.) upon tuberculosis in the guinea pig**

CONTROLS	TUBERCULIN TREATED	
	Large doses	Small doses
+++**	+++	+++
++	+++	+++
+++	++	+++
+++		

* Since the tuberculin used in this experiment failed to fulfill the toxicity requirements of officially tested preparations the results merely indicate what may be expected of tuberculins obtainable on the market. Whether potent tuberculins may not act differently was not determined.

** All these guinea pigs were sectioned on the forty-second day after infection.

TABLE 13

Effect of ether inhalations upon tuberculosis in the guinea pig

DAYS	CONTROLS	ETHER TREATED
(a*)14	++	++
30		++
51	+++	++
67	++++	+++
		+++
(b*)52	++++	++++
	++++	++++
	++++	++++
		+++

* Series a were given a subcutaneous injection of 0.0003 mgm. of culture no. 2804 virulent human tubercle bacilli, and series b of culture no. 3717.

experiment was repeated (table 13 b) ether being given daily or every other day through the entire period of infection consistent with the life of the animals. The table is self-explanatory.

The above experiments seem to indicate that ether mixed with air given daily to the point of anaesthesia for a long period of time (fifteen

to thirty days) had no appreciable effect upon the course of macroscopic anatomic tuberculosis in guinea pigs. In this connection it may be interesting to note that Graham (25) found bacteriolysis and agglutination phenomena unaffected by ether but ether anaesthesia reduces the property of promoting phagocytosis in human and rabbit blood.

Chloroform was tried by inhalation but was found highly toxic to guinea pigs if given to the point of anaesthesia so that only a few daily exposures were tolerated by the animals and this had no effect upon the course of the tuberculosis.

SUMMARY

1. A single exposure to the roentgen ray (as directed by Morton), sufficient to cause a temporary leucopenia in guinea pigs infected with a small amount (0.000,001 mgm.) of virulent human tubercle bacilli, produced no appreciable effect upon the course of the macroscopic anatomic tuberculosis in these animals. Likewise a leucopenia (as low as about 2500, as compared to a normal of about 12,000 leucocytes per cubic millimeter of peripheral blood) occasioned by the roentgen ray, existing at the time and persisting throughout the period of infection, produced just as little effect.

2. Benzene given in a single large (7.5 cc.) or repeated small (1 cc.) subcutaneous injections, had no appreciable effect upon the course of the macroscopic anatomic tuberculosis in guinea pigs produced by the injection of virulent human tubercle bacilli. Benzene inhalations once or twice daily for a period of a month to the point of anaesthesia likewise had no appreciable effect upon the tuberculosis in the guinea pigs. Benzene injected subcutaneously into guinea pigs in a mixture of an equal part of paraffine (m.p. 56°C.) is slowly absorbed, one-half remaining after the first day, one-third after the second day, one-fifth after the third day, and one-tenth after the tenth day.

3. Thorium X given in amount sufficient to maintain a marked leucopenia (as low as approximately 1500 leucocytes per cubic millimeter of peripheral blood throughout the entire period of infection of guinea pigs by the subcutaneous injection of virulent human tubercle bacilli (0.000,001 mgm.) produced no effect upon the course of the macroscopic anatomic tuberculosis in these animals.

4. Tuberculin (Koch's O. T. obtainable on the market) in large doses also had no appreciable effect upon the course of human tuberculosis in the guinea pig.

5. Ether by inhalation to the point of light anaesthesia daily for a long period of time (about a month) did not increase the susceptibility of guinea pigs to tuberculosis.

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THE TRANSFUSION OF TUBERCULOUS SHEEP WITH THE BLOOD OF NORMAL AND IMMUNIZED SHEEP

INCLUDING A STUDY OF SHEEP TUBERCULOSIS CONTROLLED BY THE COMPLEMENT FIXATION TEST

EDGAR MAYER AND DANIEL J. HURLEY

From the Trudeau Sanatorium, Trudeau, New York

Indications for blood transfusion in disease have been gradually increasing in number and, among others, toxemia now occupies a more prominent position. Accordingly, the following experimental work was undertaken to determine the influence of normal blood, and of blood containing complement fixing antibodies against tuberculosis, upon animals suffering with a progressive type of this disease.

If by immunity we imply the presence of immune bodies, that is, bodies which neutralize the toxemia or destroy the invading microörganism, then in individuals with chronic pulmonary tuberculosis those who are symptomless or almost so, may be theoretically considered to have specific immune bodies in their blood in large amounts, as a result of which they manifest a great resistance to the disease, whereas the patient with marked symptoms probably develops only few antibodies and maintains a low resistance. Investigators have attempted to increase the titre of these immune bodies in the blood of poorly-resisting patients by such means as tuberculins, dead and live tubercle bacilli, serum containing antibodies, etc., but all have proved of little value. Whole blood itself has not been given sufficient trial, while there may be something present in it that is lacking in serum alone. Libman and Ottenberg (1) state, "There is every reason to believe that in those diseases immunity to which is cellular rather than humoral, the blood cells share immune powers of other cells. The blood cells, transfused, continue to live and functionate." According to Spengler (12), "The main source of production and the chief depot of storage of the immune bodies in tuberculosis are the red blood cells. The white blood cells and blood platelets are depots of storage but not sources of production. They carry more immune bodies than the serum but less than the red blood cells. The immune bodies of the blood of immunized individuals and animals

are, in chemically pure condition, curative and prophylactic for men and animals." While the weight of evidence seems to be in favor of the cellular theory of immunity, nevertheless a considerable amount of complement fixing antibody can be found in the blood of individuals suffering with tuberculosis. Whether beneficial antibodies can, by a few repeated transfusions, be transferred in sufficient quantity can be determined only by the results; one may require only few antibodies to obtain that added stimulus for resistance which is otherwise lacking.

Our experiments were made on sheep of different ages, weights and sex. The serum was tested weekly for complement fixing antibodies with Petroff's (10) alcoholic, sodium hydrate, and potato-filtrate antigens. This test is considered one for activity or inactivity of the disease; however antibodies are often present according to the test when the disease, so far as subjective symptoms are concerned, is arrested, due probably to the fact that there is a small amount of antigen given forth from the tuberculous focus which is just enough to bring a response with antibodies, but does not cause enough absorption to give symptomatic evidence. In completely arrested tuberculosis, presumably there is no tuberculous antigen circulating in the blood and therefore complement fixing antibodies have disappeared. The antibodies, according to the tests in patients, were regularly present in chronic active disease and usually absent in arrested disease. We were able to increase these antibodies in our inoculated sheep at will by the intravenous inoculation at different intervals of suspensions of dead tubercle bacilli.

The number of animals employed in this experiment was far too small from which to draw conclusions, and the results are simply offered for what they may suggest. In carrying the analogy of the experiment to human beings, the criticism may justly be mentioned by some that it would be unfair and the risk would be too great to ask an individual with symptomless tuberculosis and positive complement fixation, to give blood by transfusion to a second person; however, the loss of blood from repeated small hemorrhages, and often from single severe hemorrhages, does not in itself appear to be of serious moment to tuberculous patients in good physical condition, so that it seems to us that patients with arrested tuberculosis can give 500 cc. of their blood with impunity.

Whole blood has been previouly employed in the treatment of tuberculosis. Hericourt and Richet (2), in 1890, reported excellent results in tuberculous rabbits treated with dog's blood. Bertin and Picq (3) reported favorably from their experiments on rabbits, using goat's blood.

Crile (4), in 1909, treated tuberculosis by transfusing tuberculous patients with normal blood and reported some improvement. At Otisville, N. Y., in 1916 (5) tuberculous patients were transfused with normal blood but negative results led to discontinuance of the treatment. Sheep were used by us, primarily, because Roemer (6) had performed serum experiments with these animals and because there had been at the Saranac Laboratory, for a number of years, an old sheep with arrested human tuberculosis; furthermore, an animal with large blood vessels was necessary for the use of the transfusion apparatus. The aforesaid sheep (afterward called no. 6) had been inoculated subcutaneously with human bacilli in 1910 and had on several occasions been treated intravenously with B. E. tuberculin. The animal had to all appearances become well and had developed antibodies in the serum as shown by the persistence of the complement fixation reaction.

PRELIMINARY STUDY

We arranged the sheep after careful observation of their characteristics, their size, vigor, and chances of withstanding repeated loss of blood, as follows: Two of the sheep (nos. 1 and 2) were males of the same age, size and weight. Sheep no. 2 we chose for the control of the animals to be infected with virulent bovine tubercle bacilli and sheep no. 1 a recipient of normal whole blood. Sheep no. 7, a female, about the same weight and size as the above described, was to be a recipient of blood containing antibodies. These three animals we inoculated intravenously (external jugular vein) with a similar dose of living bovine tubercle bacilli at the same time. They were kept under similar conditions, and were given precisely the same food and care. Sheep no. 3 was a normal female, about eight years old, which had been at the Saranac Laboratory for some years. It was the companion to no. 6, about to be described. We employed this sheep to work out our technique in transfusion, and to learn the possible dangers to the recipient from repeated transfusions. Sheep no. 4 was a large male used as a donor of normal blood, and from all available evidence had no tuberculosis. Sheep no. 5, at the onset, was chosen as a donor of normal blood but died of lobar pneumonia a few days after the first transfusion, probably because of insufficient care and undue exposure. Sheep no. 6, a part of whose history was described above, was a female, in good general condition whose blood, according to the complement fixation test, contained antibodies. This animal was chosen as the donor of antibody-blood to sheep no. 7.

The external jugular vein was employed for obtaining blood for the complement fixation tests and for the transfusions; in sheep this is a rather large vessel and, after a little experience, easily handled. Unger's (9) two-way stopcock method of transfusion was used. This required that both sheep should be fairly quiet during the procedure. Sheep although gentle will not remain motionless for a long period so that two tables with attached straps were constructed, by means of which the movements of the sheep were reduced to a minimum.[1]

The preliminary study consisted in the observation of the general condition of the sheep, their temperature, respiration, weight, complement fixation reaction, blood count and tuberculin test. The temperature averaged 103° to 105° F.; it was taken by rectum, every evening at first, later twice a day, and still later, only once daily in the morning. The evening temperature was usually the same as in the morning; very rarely it was higher. It occasionally rose to 105° F. in sheep no. 4. Respirations averaged 28 per minute but were frequently increased to 50 and on one occasion in sheep no. 4 were over 100. Their high respiratory counts seemed to us to be due to excitement.

The sheep were at first weighed at irregular intervals and then regularly once a week at the latter part of the experiment. Except for sheep no. 2, which developed a diarrhoea, all gained in weight and as soon as this animal recovered from the disturbance, it began to gain. The loss of weight in sheep no. 6 was due to the birth of twins and may be disregarded.

Every week throughout the experiment, blood in 5 cc. amounts was taken from the jugular vein of every sheep, and the complement fixation test was performed with Petroff's antigens. Up to the time of the inoculation, sheep nos. 1, 2 and 7 gave a negative fixation except with the alcoholic antigen, but positive response to this antigen is of no significance here. Sheep nos. 3 and 6 were positive four plus with all antigens;

[1] The top of the table was built to conform to the shape of the sheep. This was attached to two standards by two pivots which were so arranged that it could swing from a vertical to a horizontal position through an arc of 90 degrees. With this device the sheep were led up against the table while the top was in the vertical position and two attached straps were passed around, under the abdomen, and held by the operator who stood behind. While in this position, slight pressure was exerted by means of which the part apposed to the sheep swung from a vertical to a horizontal position, the straps firmly holding the animal and lifting it off its feet so that after swinging through an arc of 90 degrees, the sheep was lying horizontally on its side. Other attached straps were passed around the legs and head so that the animal was well held.

no. 3 until it died, and no. 6 throughout the experiment.[2] Sheep no. 6 although showing a four plus fixation, was in good physical condition and gave no symptoms of clinically active tuberculosis, so that this animal might be classed theoretically among those cases arrested symptomatically but still allowing a small absorption of antigen. Active tuberculosis in sheep is, according to R. Mayer (11), evidenced by the symptoms of "chronic slight cough, hurried respiration, fever, pallor and anemia of mucous membranes, nasal catarrh and emaciation. Such sheep are faint and weak, tire easily and lag behind the herd. They have palpably increased lymph glands."

In order to hold and raise the titre of the complement fixation reaction on sheep no. 6, it was injected intravenously every ten days with 3 mgm. of dry pulverized tubercle bacilli, suspended in normal saline solution.[3] After each injection, this sheep's temperature would rise to 105° F. or over and remain so for twenty-four hours.

Roemer (7), in his experiments, tested all his sheep with tuberculin to exclude the presence of tuberculosis. This we carried out inasmuch as the complement fixation test is considered a guide for disease activity or inactivity only. A subcutaneous dose of 0.5 cc. of old tuberculin

[2] The explanation of this positive reaction in sheep no. 3 is not entirely clear. It died rather suddenly on March 14th and showed on autopsy a pneumonic consolidation, proved by all available tests to be non-tuberculous in character.

The post mortem findings were: Right pleural cavity contains no fluid but the anterior lateral and posterior surface of the upper part of the lung is adherent to the chest wall by soft fibrinous adhesions. Right lung: Caudal lobe is not completely collapsed and non-crepitant. On section much blood is expressed. Upper half of the lung is full, voluminous, firm, and dark red. Scattered throughout the surface are whitish, opaque areas, 1 mm. in size. On section a dark red fluid with a cheesy-like material exudes on pressure from the center. Smears were taken from this cheesy material and no tubercle bacilli were found. The slides stained with methylene blue showed several microörganisms. This cheesy material planted on Petroff's gentian-violet-egg media, showed a liquefying growth. A smear from the surface showed a mixed growth. Guinea-pigs were inoculated and no tuberculosis was found. A rabbit was inoculated intravenously and after six weeks showed no pathological changes.

[3] To make and weigh out the suspension of dry, pulverized, tubercle bacilli for inoculation: Place an arbitrary amount of dry, pulverized, tubercle bacilli in a mortar and add to it slowly, drop by drop at first, normal saline solution, grinding and rubbing it up slowly as the saline solution is added. After the suspension is of the desired consistency it is pipetted off into a sterile test tube and centrifugalized for one or two minutes at moderate speed to get rid of clumps. Meanwhile, using two sterile beakers, which have been balanced on the fine scales, 0.2 cc. of the suspension is put in one beaker and evaporated to dryness in the water bath at 56°C. The beaker with residue is now weighed. This will give the weight of the amount of dry pulverized tubercle bacilli in 0.2 cc. of suspension, deducting the amount of sodium chloride in the saline solution. The dose desired to be used can be estimated from the amount of dry, pulverized tubercle bacilli in 0.2 cc. of suspension.

was given every sheep. Not receiving a satisfactory reaction in no. 6 and the suspected no. 3, the test was repeated on all with a dose of 1 cc. of old tuberculin. In no. 6 we obtained a rise of 1.5°. All the others gave no reaction. From these findings in accordance with the deductions of the State Department of Agriculture, no. 6 had tuberculosis, while the remainder were free from the disease.

We attempted many times to roentgenograph the lungs of the sheep but owing to the amount of dirt and crusts on the wool and to the configuration of their thoraces, we were unable to obtain any satisfactory plates, notwithstanding the fact that we sheared sheep no. 3. We, therefore, had to give up the idea.

Differential white blood cell counts were performed weekly at first (but later discontinued) taking the drop from the ear vein and they corresponded rather closely to the differential counts as given by Klieneberger (8). His findings are:

Total white cells	6,500
Large lymphocytes	9 per cent
Small lymphocytes	49½ per cent
Polymorphonuclears	34 per cent
Eosinophiles	6½ per cent
Mast cells	⅝ per cent
Transitionals	½ per cent
Hemoglobin	59 per cent
Red cells	11,800,000
W:R:	1: 1815

PRELIMINARY TRANSFUSIONS

The general condition of the sheep was very good, when we had completed our preliminary study. During this preliminary period we transfused several times to perfect our technique:

January 5	130 cc. of blood from sheep no. 5 to sheep no. 3
February 17	120 cc. of blood from sheep no. 4 to sheep no. 3
February 23	180 cc. of blood from sheep no. 1 to sheep no. 3
March 2	190 cc. of blood from sheep no. 4 to sheep no. 1

At first we did the agglutination and hemolysis tests, but on February 23, owing to the fact that sheep no. 4 had markedly rapid respirations and a temperature of 105° F., we transfused from nos. 1 to 3, without, by chance, performing the tests and no bad effects followed, so that thereafter we omitted them and had no disastrous results.

EXPERIMENT PROPER

On May 31, with all the remaining sheep in good condition (the deaths of nos. 3 and 5 have been mentioned) and the preliminary work finished, we inoculated intravenously (external jugular vein) sheep nos. 1, 2 and 7 with 0.0005 gram of living bovine tubercle bacilli in 5 cc. of physiological sodium chloride solution.[4] Sheep no. 2 was made the control of the experiment and sheep no. 1 the recipient of normal blood and sheep no. 7 the recipient of immune blood, that is, blood containing four plus complement fixing antibodies. Seven days after inoculation, sheep nos. 1, 2 and 7 showed a four plus complement fixation.

Two weeks after inoculation we began to transfuse. We gave little more than 250 cc. of blood at one time, because, on reaching this amount, the recipient would regularly struggle hard, although it had been perfectly quiet before the injection. Sheep no. 1 had what we considered severe anaphylactic shock after the third and fourth transfusions but was soon over it. Sheep no. 7 had symptoms of slight anaphylactic shock after the last transfusion. Both animals did well, however, and were finally killed. They outlived the control by two months.

As in the preliminary study of the sheep, so during this period, temperature, respiration, weight, complement fixation and the general condition of the sheep were followed.

BLOOD OF NORMAL SHEEP TRANSFUSED TO TUBERCULOUS SHEEP

Sheep no. 1 was transfused with blood from sheep no. 4, as follows:

June 12	250 cc.
June 23	260 cc.
June 30	200 cc.
July 7	200 cc.

Between the first and second transfusions there was an interval of eleven days and the animal showed slight anaphylaxis, so that we later decreased the interval to seven days. However, the same symptoms occurred after the second and third transfusions but were of much less intensity. On June 16, two weeks after the infection with bovine tubercle bacilli, the temperature in sheep no. 1 rose to 104° and 105° F. and remained there until the animal was killed. Until the time of its death it had not lost more than four pounds. Its respirations were 28

[4] The dose of live bovine tubercle bacilli was prepared in the same way as the dose of the dry pulverized tubercle bacilli.

and 40 per minute. The complement fixation with all antigens became four plus early and continued so to the end. The general appearance of the sheep showed definitely that it was ill. Although fairly well nourished, its eyes were dull, and its movements slow and without energy, and it assumed a sitting posture, the same that sheep nos. 2 and 3 showed for a period before they died. Its appetite was poor and its strength much diminished. It was killed 102 days after inoculation. Post mortem examination showed disseminated tuberculosis of the lower lobe with less involvement of the upper lobe. The bronchial glands were enlarged and showed signs of beginning calcareous change. Roentgenograms of the lungs removed *in toto* showed this involvement clearly.

Post mortem findings on sheep no. 1. Surfaces of the lungs are smooth and glistening. The general color of the lung is a pale, pinkish white; scattered here and there are numerous, large, translucent areas, some of them 2 to 3 cm. in diameter. These are more prominent and more evident in the lower part of the lung and posteriorly. The lung is of apparently firm consistency with consolidated areas, the size of a marble, scattered here and there; these areas are similar to the translucent ones described above. In the region of the aorta, esophagus and trachea, is a mass of firm and mostly translucent tissue, 2 to 3 cm. in width, running from the base of the lung to the apex. On section, the surface is pale and translucent with a yellowish white granular and calcareous area stretching across the surface. This mass is suggestive of glandular tissue. Smears were taken of this tissue and no tubercle bacilli were found. The spleen contains, here and there, small white opaque areas, one or two millimeters in size, suggesting conglomerate tubercles. Tissue, macerated, and inoculated into a guinea pig, showed caseous glands and disseminated tubercles in lungs and spleen.

CONTROL

Sheep no. 2 was used as a control and showed, three weeks after infection, all the signs of acute progressive tuberculosis. It moved slowly, never spontaneously as a normal animal would, and even when urged to move, responded only slightly. It quickly lost its appetite and had little strength. Its temperature rose after two weeks. There was an early loss of weight and an equally early positive complement fixation. It died July 12, forty-two days after its inoculation, and post mortem examination showed an extensive, acute miliary tuberculosis of the lung. Roentgenogram of the lungs after removal showed this distinctly.

Post mortem findings on sheep no. 2 (which died July 12). Pleural cavity contained no fluid and no adhesions. In situ, the lungs are full and voluminous with glistening surfaces. On removal, the lungs are found to be of a mott'ed, pale red and grayish color. The lungs are pale red, everywhere mottled with small, translucent areas less than 1 mm. in size, with an opaque center. These areas are scattered throughout the entire lung as seen on section. They have a firm consistency. Bronchial lymph glands are greatly enlarged, 2 x 4 to 2 x 6 cm. in size.

BLOOD OF IMMUNIZED SHEEP TRANSFUSED TO TUBERCULOUS SHEEP

Sheep no. 7 was the recipient of antibody blood from sheep no. 6. It was transfused with blood from sheep no. 6 as follows:

June 22	200 cc.
June 29	260 cc.
July 7	200 cc.

This sheep, although not entirely as active and lively as before its inoculation with live tubercle bacilli, would have appeared little different to one who did not know the animal well. Its weight did not decrease, but instead increased. Its temperature, for a short period, was a little above 103° F. but later fell below that point. The complement fixation reaction was positive on four examinations, but negative on four. To all outward appearances it was doing well. On September 12, 102 days after the inoculation, no. 7 was killed. On post mortem examination this sheep was well nourished and showed very little tuberculosis. Here and there were only occasional shotty areas of tuberculosis which were less than 1 mm. in diameter. The bronchial glands were enlarged and showed calcareous changes. The stereoscopic X-ray of the lungs removed *in toto* showed these changes.

Post mortem findings on sheep no. 7. The surfaces of both lungs smooth and glistening. Both lungs were soft, spongy, non-crepitant and collapsed, except in a posterior section of the lower lobe. This latter area is firmer than the rest and soggy. Here and there, only rarely seen throughout the entire lung, are small, greyish, translucent shot-like areas. These areas are less than 1 mm. in size. They have a yellowish opaque center with a translucent periphery. Bronchial glands are enlarged and calcareous in character. Smears from the lungs were negative and macerated tissue inoculated into a guinea pig showed tuberculosis of the inguinal glands and a few tubercles in the lungs and spleen.

Sheep nos. 4 and no. 6, the donors, are now alive and well.

CONCLUSION

In closing, it is recognized that the results are in no way conclusive, that the animals are far too few in number, that the difference in individual resistance in the same species of animals may even account for the results obtained; but we do believe that the findings are suggestive to show that normal blood on repeated transfusion is of slight value while blood containing antibodies is possibly of considerable value.

MICROSCOPIC NOTES

Sheep no. 1

Heart: negative.

Lungs: isolated and conglomerate tubercles in all stages of development; giant cells quite prominent, and *calcifications* in considerable amounts.

Spleen: tubercles in all stages of development, scattered throughout the pulp; slight calcification.

Liver: no tubercles.

Kidney and adrenals: negative.

Other organs: negative.

Sheep no. 2

Heart: negative.

Lungs: individual and conglomerate tubercles in various stages of development; *no calcification.*

Spleen: isolated tubercles scattered here and there in the pulp; considerable congestion.

Liver: congestion prominent around the central vein; isolated tubercles seen here and there in the lobules.

Kidney and adrenals: negative.

Other organs: negative.

Sheep no. 7

Heart: negative.

Lungs: no tuberculosis in these sections. (The sections of what grossly appeared as an area of tuberculous pneumonia in sheep no. 7 were unfortunately destroyed).

Spleen: negative.

Liver: negative.

Kidney and adrenals: negative.

Other organs: negative.

Sheep no. 3

Heart: negative.

Lungs: an exudate of polymorphonuclear leucocytes into the alveoli; congestion of capillaries and larger vessels.

Spleen: negative.
Liver: chronic inflammation around portal spaces.
Kidney and adrenals: negative.
Other organs: negative.

Microscopic diagnoses

Sheep no. 1. Chronic tuberculosis.
Sheep no. 2. Acute progressive tuberculosis.
Sheep no. 3. Lobar pneumonia (mixed infection).
(Sheep no. 7. Chronic tuberculosis by macroscopic diagnosis).

We express here our gratitude to Drs. Baldwin, Brown and Heise for their kind suggestions, to Mr. Petroff for his assistance in the complement fixation work, and to Messrs. Sampson and Burger for the X-ray photography.

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FOLLOWING UP THE DISCHARGED SANATORIUM PATIENT

DAVID R. LYMAN

From the Gaylord Farm Sanatorium, Wallingford, Connecticut

The beginning of the follow-up work of our sanatoria was prompted by the desire of the early institutions to furnish a skeptical public with proof that tuberculosis could be cured through their agency. When the pioneer sanatoria, such as the Adirondack Cottage Sanatorium and Rutland, first undertook to trace their old patients they did so with but one idea in view: they wanted the personal reports of the individual patients as indisputable proof of the value of the new treatment, and therefore as a basis for securing larger donations toward their work from both private and public funds. The first attempts at following up old patients were through the medium of annual letters, and these letters with their statistical data have proved of great value to all of us who have tested this method consistently, especially if we are dependent upon public funds for our support. At Gaylord Farm we have found with legislative committees, as with individuals, that our greatest asset has been the statistics of the earning capacity of our discharged patients.

Taken at the close of our first ten years of work, these showed that while $400,477.58 had been expended on maintaining our institution (including interest at 5 per cent on our construction and equipment), the discharged patients had already earned $1,339,000, or almost $940,000 more than the entire maintenance expenditure in their behalf. We were able to claim more than usual accuracy for these figures because of the fact that we had lost track of but 22 of our 1112 patients or but 2 per cent of them all.

Another statistical study which we found of great value in attracting public interest was that dealing with the occupations of our ex-patients. We divided these into two classes: those who took up new work, and those who returned to their former occupations; and classified the occupations under the subdivisions of house, factory, store, office, professional (including students), and open air. We reported our results to the National Tuberculosis Association, and based upon them our claim

that patients of the class with which we dealt did better when they returned to their old work than when they tried to find the proverbially illusive "light job out of doors," preferably on a farm. Our records showed that the factory workers held their condition distinctly better, and the office workers far better, than did the outdoor workers. It was a great satisfaction to me at that meeting to find that Dr. Vogeler, at Sprain Ridge Hospital, Yonkers, had been carrying out identically the same investigation among his discharged cases, and with a classification so nearly like ours that one could have been substituted for the other. The fact that his results exactly paralleled our own and that the two investigations had been made entirely independently, added greatly to their value. I mention these records in particular to illustrate the value of such data when kept by many sanatoria; for it is only through a study of such records from several sources that we can get a proper perspective from which to study our problems.

The need of such records for more accurate comparison of results among ourselves was recently illustrated for me by an exhaustive set of tables sent us by Dr. Rathbun, and dealing with the follow-up statistics of Otisville patients returned to New York City. I had often wondered just what was the real reason for the discrepancy between their after-results and ours. Theirs had been so unsatisfactory as to imbue them with the idea that these patients must be colonized outside of New York and favorable occupations found for them. Our data, on the contrary, have furnished convincing evidence that our problem in Connecticut was largely one of early diagnosis and of supervision after discharge, and that as a rule it was not necessary for the patient to change either his residence or his occupation. It was evident that Otisville and Gaylord Farm were dealing with very different problems; but I did not realize how different until I glanced through the tables sent me by Dr. Rathbun and found that the average weekly earnings of those of his patients who were working was $9.81. That struck me as so much lower than our own that I looked through our follow-up letters for this year to see what information they would give me. Of 344 men who had stated their earnings, only 13 were earning ten dollars or less a week, though this was the average earned by the Otisville cases. Two-thirds of my men were earning over $15.00 a week, and the average for the 344 was $21.37 a week.

As regards the women, we had made (as Otisville had also) an allowance of $9.00 a week for women doing their own housework; and in-

cluding these, the average earnings of all of our women was $10.20 a week as against $9.81 for the average of all the Otisville cases, both men and women.

Of course our data this year show exceptionally high earnings for we are in the center of the brass and the munitions industries, and the wage scale is much higher than normal. However, the comparison of our data with Otisville shows that we have an infinitely better problem to deal with both as regards education and living conditions as well as housing, and goes far to explain the discrepancy in our results.

To give one more evidence of the value of such data, let me report the results of an inquiry added to our blanks this year. We hear much of the objection to sending patients to sanatoria because of the injury it will do them later through the prejudice of their fellow-workmen. It has always seemed to us that this phthisiophobia was not so marked as generally supposed and yet we had no data on the subject. We therefore asked each of our old patients this question, "Has the fact that you have been at a sanatorium given rise to any unpleasant experiences with your neighbors or fellow employees?" Six hundred and thirty-three answered this question: 590 stated that they had never had any trouble of the kind, and quite a few of the 43 who reported such experiences stated that they had been of a very trivial character; in other words, the facts as shown from these letters are quite different from the general conception of the situation.

This form of follow-up work by the use of annual letters and questionnaires can bring us most valuable statistics, and I would strongly urge its adoption where better and more effective measures are impossible. Incidentally I would mention the fact that we have found the plan of holding reunions of old patients of great aid in maintaining their interest in us and in securing replies to our letters. At out last reunion three years ago we had over two hundred old graduates back to see us, and this year we are expecting double that number.

In recent years we have begun to realize that no public health work can be brought to its highest development until it is carried to the people in their homes, and not made available only for those who can be brought from their homes under its influence. We have seen this with school hygiene and with infant welfare work, but nowhere does it hold more true than in the tuberculosis campaign.

We all of us know that many of our patients leaving us with a thoroughly arrested disease relapse within one or two years; and in the ma-

jority of these cases we know that the relapse could have been avoided with proper care. We know that carelessness is the chief cause of the failure of our seemingly good cases, and that we must do away with this carelessness before we can get our best results. Returning home from a long period of sanatorium treatment, most patients will be careful for about six weeks, a moderate number for six months, but only an occasional individual for six years. This tendency to carelessness increases in direct ratio with the length of time the patient has been away from sanatorium influence (or supervision), and is complicated—indeed, is often aided and abetted—by the attitude of the family and the neighbors. This attitude is usually founded on an entire ignorance of the subject or of the needs of the patient and a sublime confidence in their ability to determine what is best for the patient under any and all conditions.

We often speak of our institutions as training schools, claiming that the educational feature of their work is the most valuable of their functions. This is true, but it is also true that in order to secure permanent results it is fully as necessary to educate the family as the patient, and so far we have made but little effort to do this.

While this is not strictly follow-up work, it is so closely allied to it that I feel justified in presenting it briefly to your attention. In fact, in our experimental work in employing a visiting nurse to keep in touch with our old cases, we have found this feature perhaps the most valuable of all her activities.

In order to insure the patient the best possible chance after his discharge from the sanatorium, we have tried to carry our work to his home and to get the education of his home circle well started before his return, instead of leaving it all to him to do afterwards as heretofore. We have found that our nurse can accomplish a great deal in this way. To begin with, she resides at the sanatorium and makes it her business to make friends with the new patient and to get acquainted with his family on visiting days. When later the question develops of visiting his home so as to see just what facilities there are available for his after-care and to advise as to their best usage, the proposal comes from a personal friend and is welcomed accordingly. Once in the home the nurse has ample opportunity to explain fully the coöperation which the family must give and the importance of its attitude toward the patient and his daily routine.

We have found that the nurse can do much more than this. We all know that her visits are our best means for locating unsuspected early cases in the family circle, but I for one have only recently realized what an aid she can be in securing important data on the patient's personal or family history. I find that she brings me data which the patient had either forgotten or deliberately concealed. I have several cases where the patient gave a negative family history but where the nurse has, as the result of a little gossip in the patient's home, brought me a story of definite exposure in childhood. She also gives me useful sidelights on the character and idiosyncracies of the patients and unearths personal and family worries which are a great drawback to a successful "cure," and which we can often alleviate. Add to all these the fact that these visits establish personal relations between the sanatorium and the patient's home, which make it easy to keep in touch with him after discharge, and you can readily see the very great benefit this work can be to the patient, the institution, and the community.

The follow-up work of the present day is a development far in advance of the annual circular letter of our earlier efforts. It has two distinct aims. Primarily it seeks to procure more permanent results for the patient. Secondarily, it is intended to aid us in amassing data on housing, living, and industrial conditions, which data shall be the recorded observations of trained investigators and not the haphazard replies of those who look upon our questionnaires as nuisances, impertinences, or both. This second function of our follow-up work must be further developed to give us the correct answer to many of the questions which confront us. To control tuberculosis in any locality we must know the chief determining factors of the incidence of the disease in that locality. These may lie in the housing facilities or in the industrial conditions, or in the habits of life of the population (the problem usually varies with the locality), but this can only be determined by careful study in the homes of the cases which come under our care.

Such statistical studies are, however, as I said before, of secondary importance. The great value of follow-up work lies in its influence in prolonging the life and working capacity of the patients.

It is generally recognized that all people do just a little bit better when they feel that they are under observation than when left to their own devices. The patient who knows that his doctor or the nurse from the sanatorium is likely to come around asking his family about his mode

of living, is much less liable to take to late hours and bad habits than the one who is under no such control. These follow-up visits also often result in detection of symptoms of relapse before serious damage is done. Left to himself the patient is usually inclined to put off doing anything about a slight return of fever, a loss of "punch," or even a slight hemorrhage, and prefers to "take a chance" in the hope that the symptoms will disappear. The visiting nurse is very often able to persuade such patients to seek medical advice at once and thus ward off serious relapse. Since our old patients have learned that we have a visiting nurse we often have ex-patients send us word that others who were in the sanatorium with them are becoming careless, are running active symptoms, or are in need of assistance which we might be able to give. The unwritten law of secrecy as to the ways and deeds of one's fellow-patients does not (fortunately) extend beyond the term of residence in the sanatorium, and the nurse can rely upon the aid of quite a corps of voluntary assistants who will bring her most valuable information.

I recently had the pleasure of going over the follow-up work of the trustees of the Massachusetts Hospitals for Consumptives, and was especially interested in one feature of their very comprehensive campaign. They are paying especial attention to the family physician and making every effort to secure his coöperation. They are also utilizing all local agencies, where these exist, such as tuberculosis associations, visiting nurses associations, Red Cross public health nurses, boards of health, etc., and are endeavoring to avoid all that duplication of effort which is so often evident in our public health work.

When a patient is discharged from one of the Massachusetts sanatoria, the superintendent sends to the central office of the trustees a brief résumé of the case, giving the condition on admission and on discharge, the reason for discharge, and any data as to personality, home conditions, or other factors having a special bearing on the case. The central office files this statement, but sends copies of it to the patient's physician as well as to the executive officer of the local tuberculosis association and to the visiting nurse if one be fortunately available. Where there is any local agency to make regular visits to the patient's home, the central office is careful to let it do this work, but asks it for regular reports on the conditions as found. Where no local agency is available, a nurse from the office of the trustees makes these visits; but whatever the agency through which the patient is reached, a report of the visit is at once sent to the patient's physician, and if conditions are present which

can be bettered by his assistance he is asked to drop in and lend a hand, and then report in turn to the central office.

Our experience has been that it is very difficult to get patients to remain under the supervision of their doctor after they return home. We have tried to secure this by sending the family physician copies of the notes of all examinations while the patient is under treatment, and then advising the patient to keep track of his temperature and weight and submit a record of these to his physician at least every two weeks for the first few months after discharge. We find it hard to get patients to do this for most of them do not see where the benefit to them would justify the expense of these visits, and many judge the value of the general practitioner in the after-care of tuberculosis by his record as an early diagnostician of the disease. Such medical supervision is, however, of greatest benefit to the patient, and the Massachusetts system seems not only most likely to secure this but is also calculated to insure a continued interest in the case on the part of the physician himself.

With the local boards of health, the physicians, the charity organizations, visiting nurses, and local tuberculosis associations, all working in coöperation with the central administrative office, it should be possible to keep the majority of our patients under fairly regular supervision after their return to active life. The increase in length of life and in earning capacity of our patients would pay the cost of such a system many times over, and the accurate data we would be able to gather might be the means of advancing our work against tuberculosis beyond its present almost stationary position.

WHEN DOES AN INDIVIDUAL BECOME A CASE OF TUBERCULOSIS FROM A BOARD OF HEALTH POINT OF VIEW AND WHEN DOES HE CEASE SO TO BE[1]

JOHN B. HAWES, 2ND

Boston, Massachusetts

The question that I have been asked to discuss, as to when the tuberculous person becomes a board of health problem and when he ceases so to be, is one that at first sounds simple enough. Tuberculosis is a reportable disease and the natural answer to this question would be that every case must be reported as soon as the physician becomes aware of the fact that the patient has tuberculosis, and likewise, the patient is no longer a board of health problem as soon as the physician honestly feels that he no longer has tuberculous disease. It is, of course, evident that this question cannot be answered as easily as this. We are at once confronted by the two terms, tuberculous infection and tuberculous disease, and by the vast number of patients whose tuberculosis lies in that somewhat indefinite region between infection and disease. And again, we are up against the fact that no one can be really proved to have tuberculosis of the lungs until bacilli have been demonstrated in his sputum.

My own opinion in such a big question as this is of little value; nor is that of any one man. I have, therefore, endeavored to get an expression of opinion from various men, hoping that thereby I might present a composite point of view from a group of clinicians, whose opinion taken thus collectively should bear considerable weight. I have made a brief summary of what each of these men has written or said to me on this subject, which I present here in alphabetical order. Any opinion, coming from such a group as this, should be given careful consideration.

Dr. Edward R. Baldwin, Saranac Lake, New York. To sum up my judgment, the reporting of tuberculosis should be confined to open cases, and in closed cases only those in which there is *no question* but that the disease is active.

[1] Read by invitation at the meeting of the Massachusetts Association of Boards of Health, July 25, 1918.

This of course leaves a wide margin for definitions of "activity,"which might be embarrassing from the health officer's standpoint. The danger of any other rule, in my opinion, is that many innocent people will be called tuberculous when there is no definite proof that they have the disease.

Dr. Baldwin takes, what I believe to be, a sound and conservative point of view. I feel sure, however, that there are many, who will not altogether agree with him.

Dr. Harry Lee Barnes, Wallum Lake, Rhode Island. All individuals having symptoms resulting from tuberculosis of the lungs should be reported to the boards of health. If the physician is sure enough of the condition to make a positive diagnosis, then the board of health is entitled to a report. A case in which tuberculosis is merely suspected or doubtful should not be reported, and one cannot specify just what combination of symptoms and signs make the diagnosis certain. If only patients with positive sputum are reported, the value of registration is greatly reduced, as in many patients the sputum changes from negative to positive in a short time, and all persons having tuberculosis and symptoms resulting therefrom need supervision even though the sputum is negative. Registration cannot be restricted to "active" cases without confusion, as some chronic patients who are a menace because of positive sputum are quiescent or inactive for years under ordinary conditions of life. The standard adopted by the National Tuberculosis Association for use of the words, "apparently cured," requiring complete freedom from symptoms and bacilli for two years, might be a good one for boards of health in deciding when to discharge from observation in follow-up work. Cases relapsing would again be reported and followed up.

Dr. P. Challis Bartlett, Framingham, Mass. I consider every active case of tuberculosis of the lungs a case of tuberculosis from a board of health point of view. Such a case, whether or not there is a positive sputum, I consider a board of health problem because he may be infectious at any time if not properly cared for. The fact that no tubercle bacilli are found in the sputum by ordinary examinations is no proof that they do not exist.

I consider a patient ceases to be a board of health problem when the signs of active disease have disappeared and symptoms have disappeared, in other words, a case of apparently arrested disease. If such a case again shows symptoms it should be reported to the board of health and followed as in the first instance.

Apparently Dr. Bartlett does not believe that the attitude of the board of health should be any different toward a case with a positive sputum, from what it is toward the case with a negative sputum. I am inclined

to think, however, that when a physician reports an incipient case of tuberculosis with no sputum at all, or with a negative sputum, that the attitude of the board of health might well be different than it is toward the more active and progressive case.

Dr. Vincent Y. Bowditch, Boston, Mass. I am in favor of reporting every case of tuberculosis provided the physical signs and personal history are such as to make the diagnosis positive, regardless of the fact that tubercle bacilli may not have been found in one, two, or even more examinations of the sputum. I believe the advantage to be gained by notifying the board of health in all cases far outweighs the possibility of a wrong diagnosis with its attendant discomfort. At the same time, I believe all such cases should be treated with the greatest consideration and kindness, avoiding the unnecessary publicity and lack of tact (to say the least) that is sometimes shown by agents who are sent to visit reported cases.

I think it quite impossible to place any definite limit of time as to when a patient ceases to be considered as a "health problem." If a patient while under observation remains for a number of months (for the sake of having a definite figure, say *six*) without cough and sputum and in apparent health, he might easily be considered as beyond the jurisdiction of the boards of health; certainly, if under the eye of a competent medical man.

In the event of a patient's returning to his home physician after a successful sojourn in a health resort or sanatorium it would be well for his physician to report his patient's condition to the board of health if for nothing more than the value and interest of classified record, and, *provided* that the patient remains under the eye of his physician, I think it better that he should *not* be followed up by the board of health on account of unnecessary annoyances to the one most concerned, unless he shows signs of *relapse*, in which case, I believe that notification should again be made and if the patient does not show proper regard for his own welfare and that of others he should certainly come again under the jurisdiction of the board of health.

Dr. Bowditch has evidently had experience with patients who have been subject to annoyance, to say the least, by the repeated visitations of over-zealous agents and nurses of the board of health. The consideration and kindness and the avoidance of unnecessary publicity, which Dr. Bowditch urges, are certainly of the greatest importance in handling such cases.

Dr. Lawrason Brown, Saranac Lake, New York. In regard to reporting only patients with a positive sputum, I feel that a great many patients, who usually have no cough or expectoration, would show tubercle bacilli in the sputum dur-

ing a little cold if you examine it. To press this point logically would mean that every patient ought to be considered more or less a menace to the public health as long as he has any cough or expectoration, and only when his cough or expectoration has been absent for three or four or six months should one remove his name from the list of the board of health. I feel that so many cases of pulmonary tuberculosis relapse, that one ought to be guarded before telling a patient that he is no longer a menace to other members of society; in fact, I should consider it wise to tell him that if at any time he has a severe cold, he may stir up some old trouble and so have tubercle bacilli again in his sputum. After a patient returns home and is without symptoms for some months, I certainly see no reason why he should be under supervision by the board of health, unless he should grow worse.

Dr. Brown evidently feels that every patient on whom the diagnosis of tuberculosis is made should be reported and that the physician should hold himself in readiness at all times to report any arrested cases that may suffer relapse.

Dr. Henry D. Chadwick, Westfield, Mass. First, I think a person having physical signs and symptoms indicating clinical disease, with or without positive sputum, should be reported. Second, a person having physical signs, although without symptoms of active disease, but with positive sputum, should be reported. Then one must consider the significance of clinical symptoms, considering carefully malaise, fever, loss of weight, as indicating constitutional disturbance; cough, pleurisy, hemoptysis, as showing the location of the disease. All these symptoms except cough indicate an active process. It should be remembered that cough may continue for a long time in inactive and well arrested cases.

I will say, therefore, that when one or more of these symptoms are present and cannot be explained by other causes than tuberculosis, together with characteristic changes in the lungs, such a person should be reported. As soon as a case is diagnosed and reported, such a person should be followed up and any change of residence of such a patient should be made known to the health authorities. This surveillance should last until the patient has well arrested disease and ceases to be a carrier or spreader of bacilli.

A well arrested case of pulmonary tuberculosis, without symptoms, is in the same class as an infected child without symptoms of the disease. Neither case is a menace to public health and it seems to me need not be kept under observation by the health officials and should not be classified with the cases of active tuberculosis in the community. We are rapidly coming to realize and to face the fact that all humans have more or less tuberculosis at some time in their life; therefore, we should list only those cases who are or are likely to become infectious to the community in which they live. It seems to

me that this is the common sense view point to take with regard to the law requiring a report of cases of tuberculosis.

Dr. Chadwick, I think, states this whole question in a very fair and sensible way. I agree heartily with his point of view.

Dr. Sumner Coolidge, Middleboro, Mass. Personally I should report every case as soon as I made a diagnosis in my own mind.

As soon as a case becomes an arrested one, he ceases to be a health problem so far as being a menace to others, but I believe that every such case should be under surveillance and a report called for at intervals so that boards of health may be informed if he breaks down; such surveillance to extend over a period of two years at least.

Sending a patient to a recognized sanatorium or hospital for tuberculosis should be considered *prima facie* evidence that a diagnosis of tuberculosis has been made, and that the case should be reported to the board of health.

Dr. Cleaveland Floyd, Boston, Mass. I feel that tuberculosis is distinctly a board of health disease and that it should be under observation by the board of health from the time the disease is proved or suspected until the patient is well for a period of five years. I set this latter figure to cover relapses and to allow oversight of the family. Too little supervision of the active sort is exercised by any but a few boards of health.

Dr. George N. Lapham, Boston, Massachusetts. At the present time it is evidently up to the physician to rely on his own judgment as to whether a patient shows sufficiently definite symptoms and signs to warrant his reporting the case. Many physicians appear to be content with one negative sputum report. This is often misleading and unsafe, for we know that it frequently happens that tubercle bacilli are not found until after repeated examinations, if at all.

I believe that cases, other than those having tubercle bacilli in their sputum, should be reported:

1. When the patient gives a history of gradual onset of unusual fatigue and slight or considerable loss of weight, persistent P. M. temperature of 99.2 or over and persistent localized râles at either apex, *with* or *without* cough.

2. Cases of definite hemoptysis (otherwise unaccounted for) even in the absence of symptoms.

For the returned cases one or the other of two courses should be followed:

1. They should remain under care of their physician who must satisfy himself that the patient is taking all due precaution to protect himself and family; or

2. If the patient is not taking due care he *must* come under the supervision of the board of health, which will force him to do so, or, if he is incorrigible, send him to some institution.

Dr. E. O. Otis, Boston, Mass. So far as the community is concerned, the main purpose of reporting cases is the prevention of the spread of the disease and from this point of view any case without tubercle bacilli is not a menace to the community and logically would not be a reportable case. There is always the risk, however, that at any time tubercle bacilli may appear. I therefore report all cases in which I have made a *definite* diagnosis of active tuberculosis to my own satisfaction whether or not tubercle bacilli are present. When, however, there is any doubt in my own mind as to the diagnosis I keep the patient under observation but do not report it. In reporting active evident cases, but without bacilli in the sputum, it would be wise to state that fact, for so long as bacilli remain absent the case is not a board of health problem provided it is under the observation of the physician.

When the case is arrested, I see no reason why one should report it again or it should be under the surveillance of the board of health. A case, arrested to the satisfaction of the physician is not a menace any longer to the community. Of course the fact might be conveyed to the board of health that the case has returned "cured" or "arrested." I have been beseeched by returned cases, able to take up their duties again, to stop the continued visits of the board of health agents; perhaps a closer relationship between the physician and the board of health might obviate such unpleasant occurrences.

When a case returns, however, from the sanatorium or elsewhere which is not arrested, and is still active—as many cases do—it should again be reported by the physician if he is consulted by the individual or is cognizant of the fact.

Dr. Robert C. Paterson, Saranac Lake, New York. In my opinion it is impossible to draw the line between cases of clinical tuberculosis which are a menace to the community and those which are not dangerous. Open cases certainly are a health board problem; but it is impossible to decide what cases are open and what closed as any case that has any sputum at all is probably at times open, although repeated examinations be negative. One case in point occurred here in which the fifty-seventh examination revealed bacilli. It, therefore, seems necessary that all cases which are diagnosed as tuberculous should be reported and thus become a board of health problem. Just what the board of health can do without infringing on the much talked of "personal liberty" of the patient is a question for it to solve.

The last part of your question, "When does a patient cease to be a problem for the board of health?" can only be answered in a theoretical way, and that is, that he is always a problem if he has ever been one. We know pretty well that a person who has had tuberculosis of sufficient extent to give symptoms, and become, therefore, a clinical case, always harbors living bacilli in his system, and will in 85 to 90 per cent of cases eventually die of tuberculosis. Many cases after arrest still have bacilli in their expectoration and are to be

considered in the same light as diphtheria or typhoid carriers, although the majority of these patients, after having received their education in sanatoria or health resorts, will take care of the irexpectoration in such a way as to be of little danger. It must be remembered that there are cases who will have bacilli, during the course of a common cold, which will disappear with the subsiding of the acute infection. My own practice is to report every case which I put down on my records as tuberculous whether it is a case recently diagnosed, or a patient coming from some other health resort, who has been under treatment before. In this way I protect myself and it is up to the board of health to determine whether the case is a new one, or is merely reported from a different locality.

Dr. Olin S. Pettingill, Hebron, Maine. I think every clinically active case of tuberculosis should be reported to the local board of health as soon as the diagnosis has been made. I do not mean cases of apparent or so called tuberculous infection, but those where actual tuberculous disease exists.

All cases of pulmonary tuberculosis with tubercle bacilli in the sputum should be under the supervision of the board of health and remain under observation as long as there are tubercle bacilli in the sputum. A case will certainly cease to be a health problem when it conforms to the health requirements of an "apparently cured" case as defined by the National Tuberculosis Association. There should be negative sputum or no expectoration in positive cases for a year and perhaps longer before discharged from the books of the board of health.

Dr. Charles O. Probst, Columbus, Ohio. I believe that we should consider only "open cases" as problems for boards of health if we could be sure that our "closed cases" would not soon become "open cases."

I can see no very good reason for reporting an arrested case with a negative sputum to a board of health except for statistical purposes.

Dr. Arthur K. Stone, Framingham, Mass. I feel first of all that all open cases of tuberculosis, with bacilli, belong to the board of health; that all closed cases who need institutional care, are during that time, together with their families, under the charge of the health board; that arrested cases, without bacilli, who have been charges upon the local board of health should be reported on leaving the institution; that after suitable observation by the dispensary in the town, they then should be formally certified to the overseers of the poor as having passed from the jurisdiction, as far as financial aid goes, of the board of health. This does not relieve the patient of necessary visits to the dispensary, or of occasional home visitation from the dispensary nurse or other visiting agency. This medical supervision should be kept up for at least a year after discharge as arrested from any of the state sanatoria. The fact that the arrested case is unable to entirely support himself or to provide for the support of his family I do not believe belongs to the work of the

health boards. This statement is made to meet the existing laws of the Commonwealth of Massachusetts.

Although these various opinions as here expressed, differ in some minor details, there is to be noted a general agreement along certain lines. I would, therefore, summarize as follows, what I feel to be a fair statement of what this group of clinicians, including myself, believes to be a right and proper course concerning the reporting of cases of tuberculosis.

1. Every physician should report, and the board of health has a right to demand such a report, concerning every case of tuberculosis with bacilli recently demonstrated in the sputum.

2. The physician should report, in addition to this, every case in which he honestly believes the diagnosis of active pulmonary tuberculosis to be justified.

3. The board of health has a right to request, but not to demand according to law, information concerning every other case of tuberculosis in which the diagnosis is clear, even though tubercle bacilli cannot be demonstrated in the sputum, and even though there may not be marked signs of activity. The attitude of the board of health toward this last group of cases, which should be a large one but which, at present, is a very small one, must be determined by the individual circumstances surrounding each case.

A patient with, or having had, pulmonary tuberculosis ceases to become a board of health problem when:

1. Bacilli can no longer be demonstrated in the sputum, by repeated examination, after a period of at least two years.

2. When the board of health has knowledge, satisfactory to itself, that the patient's own intelligence and precautions and the supervision of the patient's physician are such as to no longer render him a menace to public health.

These statements that I have here made must simply stand as suggestions representing, as I believe they do, the opinion of men whose experience has been considerable. I hope that they will form the basis for discussion so that a definite, practical and sensible stand on this most important matter can be taken.

A STATE PROGRAM FOR THE ERADICATION OF TUBERCULOSIS

H. W. HILL
Old Capitol, St. Paul, Minnesota

May I say that in presenting this paper I am speaking as an individual and not as Executive Secretary of the Minnesota Public Health Association. I say this simply because I have returned to my work in Minnesota so recently that it has not been possible to consult the general membershp of the association, or to secure a pronouncement from the association on this subject.

My assigned topic, the "Eradication of Tuberculosis" once the "mere dream of crazy fanatics," is now a perfectly sane subject for sober business-like discussion, and this fact in itself is the most heartening one that I know to present to you as co-workers, soon to be co-victors, over this ancient enemy of mankind.

Another most heartening consideration is this: we now really do know *how* to eradicate tuberculosis. Our problem is not now one of our own ignorance, but of administration; not of principle but of method; nor even wholly of method. Really it is the problem of choosing the best of several methods, all workable in some fashion; perhaps each one the best one, in particular instances.

A state program for the eradication of tuberculosis can differ from any other program for any other unit merely in administration, not in principle, and I will therefore recapitulate these principles briefly for the sake of building up from a firm foundation.

We recognize two distinct forms of tuberculosis in man, one found chiefly in cattle (the bovine), the other found chiefly in man (the human). Of these two, the bovine affects man chiefly in childhood; the human affects man chiefly in adult life; the bovine is confined largely to parts of the body not communicating directly with the outside world, and is therefore practically non-infectious from man to man; the human chiefly affects the lungs and, therefore, by mouth-spray, sputum, and hands, is infectious from man to man in a proportion something like ten times the infectiousness of the greatly over-dreaded leprosy. The bovine is eradicable completely from the human race by boiling all cow's milk before

use as human food; the human disease is eradicable from the human race only by the prevention of the spread of infected excreta from the infectious or open case unless, indeed, the at present very unlikely but very much to be desired ideal be some day reached, that of a truly protective serum or vaccine or other real immunizing agent.

The program for eradicating bovine tuberculosis from the human race is a ridiculously simple program, since we know that heating cow's milk universally before use as food is all-sufficient. We anti-tuberculosis people should, I think, as a body, pass a strong resolution recommending absolutely compulsory pasteurization (or even simple boiling) of all cow's milk for all households, and we may do this now without qualms, for all the best pediatricians or children's specialists everywhere have at last overcome their fears of the evil effects of pasteurized milk on infant nutrition, and are now actually requiring that all cow's milk for all human babies shall be boiled. The raw milk of today is a relic of the raw views of our uncivilized progenitors, and we who at least pretend to strive after real civilization should cast it from us together with the unscreened outdoor toilets, the sewage-polluted water supplies and other similar barbarities of our savage forefathers. I need hardly add that killing bovine bacilli before swallowing them, thus advocated, will also kill human bacilli which may have been deposited in the milk, to say nothing of other infective germs often present. Hence every anti-tuberculosis worker should be, as a matter of course, an anti-raw-milk propagandist also.

Eradicating bovine tuberculosis from the human race is, therefore, a simple, almost ridiculously simple procedure, and necessitates only the boiling of the infectious product before admitting it to our bodies.

But the eradication of human tuberculosis from the human race is much less simple, because we are here confronted by the sad fact that the infected product presented to us cannot be boiled before it enters our bodies. It does not come to us *en masse* in a glass or metal container, but in fine droplets scattered through the air when the patient sneezes, coughs, or even talks; in fine films smeared upon his hands; and so on ours; in messy gobs stuck to the soles of our shoes. One of the curious examples of the back-end-to progress of human appreciation of physical facts is the belief that sputum in masses that can be seen and avoided were at first considered to constitute the great danger, while the insidious and much more dangerous, because unseen, mouth-spray and hand-smears were for years wholly overlooked.

This physical difference in the respective vehicles by which bovine bacilli and human bacilli are respectively carried from their sources in the living body is the ultimate basis of the administrative difference in the problems presented by these two varieties of tuberculosis.

We may compare the infectiveness of bovine tuberculosis with the infectiveness of typhoid fever, both yielding the infective material in large masses easily sterilizable. But human tuberculosis of the lungs parallels in infectiveness scarlet fever, diphtheria and other mouth-borne infections, which depend for their spread upon fine particles shot into the air, and upon invisible smears on hands.

Typhoid fever disappears as soon as the infective excreta are refused entry to the human mouth in a raw condition; so bovine tuberculosis. Scarlet fever and diphtheria remain with us so long as mouth-spray and hands play their part unchecked; so human tuberculosis. But human tuberculosis is in some ways more amenable to control than scarlet fever or diphtheria.

Scarlet fever and diphtheria are infective early in the disease, even before the disease can be recognized; and to this fact more than to the existence of carriers is due their continued presence in even those communities which are seriously trying to eradicate them.

Human tuberculosis may, however, be detected long before it becomes infectious. Moreover, the existence of carriers in tuberculosis has not yet been definitely established.

Hence the eradication of human tuberculosis by the method of isolation of the infectious individual is a more practical proposition, promising larger returns in reduction of infection, than is isolation in other infectious diseases, effective as isolation is in these other infectious diseases, when properly carried out.

We may assume then, that until that glad day when a reliable immunizing agent against human tuberculosis may shine forth upon the world, our only real weapon against human tuberculosis is the isolation of the infectious cases.

Our basic program therefore resolves itself into this as the central point, all other correlative measures being indeed only correlative and subsidiary to this one, the isolation of the infective individual.

I think, so far, we are all practically agreed. But the question of how best to arrive at the prevention of infection from the infectious case has split the tuberculosis world into two camps: the one desirous of finding the infected man before he is infectious, then treating him so that he

never becomes infectious; the other, and at first sight less plausible school, demanding that administrative action be concentrated on the case which is already infectious. The former method appealed more to public sympathy in earlier days, because the appeal was to save the sick, to save an obviously threatened life, rather than to do something intangible, almost abstract, like preventing the spread of infection. The early case promised a far greater percentage of tangible returns, that is, of recoveries. To this day the early, curable case is, very naturally, the favorite of the average sanatorium man, who wants to see definite results from his work, who wants to save the individual patient committed to his care; and he cannot well be blamed for shrinking from the care of those later cases who are practically already doomed to die.

But like almost all human impulses when based on emotion, however generous, this instinctive turning to the early case, and letting go of the late case, have truly proved on cold-blooded analysis the way to save the individual, but alas, at the expense of the race. We now see that the anti-tuberculosis movement must proceed upon the larger, loftier, and, it must be said, colder-blooded and more calculating plane of humanity to the whole race. In brief, we must, as I see it, neglect, comparatively at least, the early case so far as sanatorium treatment is concerned and concentrate upon the advanced case, if we are really to eradicate tuberculosis.

I have, in deference to common usage, used the terms, early and late, as if they meant something to public health. But let me here emphasize once and for all that from the public health standpoint these terms are correct only in a most general and indefinite sense. Whatever clinical classifications may be used, the true public health classification of cases, is into infectious, or open, and non-infectious, or closed. The infectious case, however, clinically classified, requires isolation so long as he is infectious; the non-infectious case, however, clinically classified, is harmless while he remains non-infectious.

What then would be my state program? First, the provision of isolation facilities for the infectious cases, and second, the segregation of these cases therein. We have, I think, a general average of approximately two such infectious cases per thousand of the population, and that means we need a hundred-bed sanatorium for each fifty thousand persons. Inasmuch as our populations are not distributed in fifty thousand lots, and inasmuch as the county populations in many cases approach to such a population, or can be combined together to make

such a population, I think the county sanatorium for the advanced cases, in the proportion of 100 beds to 50,000 population, is the ideal. This would mean in Minnesota about 40 to 50 such sanatoria, scattered amongst our 86 cities. We have to date approached this ideal to the extent of 14 sanatoria.

What should be done with the non-infectious case, especially the early non-infectious case? This, I believe, should be trained at the sanatoria for open cases, in buildings situated on the same grounds but separated from the open cases. Residence in these institutions for the non-open case should be avowedly for educational purposes. It is often advocated to teach the open case at a sanatorium so that he may go home while still open, and yet be harmless because he now knows how to prevent infection of his associates. This is a dangerous delusion, a snare, and an impossibility in ninety-nine cases out of every hundred, another example of back-end-to estimation of the needs of the situation. But to train the non-infectious case how to live for his own best interests is possible, practicable, and a reasonable solution of the sociological difficulties.

It has been said that it is impracticable to house all the tuberculous, that we must call a halt on sanatorium buildings, that the race cannot endure the expense; and so forth.

I agree that we cannot house *all* the tuberculous in sanatoria; if we attempt it, the race is doomed to financial disruption. But we can and must isolate, preferably in sanatoria, all the tuberculous *who are infectious*, and if we do not the race is doomed to continue tuberculous as one of the joys of living for centuries to come.

I believe we have overdone the attempt to hospitalize the non-infectious case but I equally believe we have under-done very much the attempt to isolate the infectious case.

These county sanatoria, established at the rate of about 100 beds per 50,000 population for open cases, together with sufficient beds for the non-open cases, should be more than the anti-tuberculosis center of the county. They should supervise the county unit for health propaganda in general, the center for tuberculosis clinics truly, but also for child welfare clinics, for adult clinics, for school clinics, and in general for all other health efforts of the county or counties associated together.

Thus I believe a series of such consolidated health centers, if you like, can be provided, with a minimum of physicians, nurses, and beds, and a maximum of efficiency. These county health centers should be under

state supervision, and that state supervision should be strong, unified and progressive. The controlling policy should be centralization of principles of action, decentralization of the action itself. Independent control would be a total failure; so also a centralized staff attempting to operate from a distance must in the long run fail. Centralized control with decentralized operation,—that is the proper motto of all big business.

If I may summarize, my state program for the eradication of tuberculosis is:

First, the education, now very well done, of the public needs, then the establishment of county centers, not exclusively for tuberculosis, but for all health work, with facilities for handling all serious infections, but, of course, chiefly, for tuberculosis in the open stage. Such cases should be sought out and isolated ruthlessly until non-infectious.

As a secondary consideration, but as a very close second, accommodation should be provided for the treatment, but more particularly for the education, of the non-infectious tuberculous. Clinics, dispensaries, and a follow-up system, covering the county, should be provided by the county sanatorium staff; and state supervision and control should correlate, unify and standardize the work. Please understand that while patients at such a sanatorium should be largely tuberculous patients, the work of a staff throughout the district would include all health endeavors, child welfare, prenatal care, medical school supervision, venereal disease clinics, etc., a real health center for the county, including ultimately, and as a necessary part of the anti-tuberculosis program, the periodical examination of the whole population.

May I briefly enumerate the advantages of this plan:

1. Economy in operation, since the multiple efforts in many health directions now made by separate staffs and organizations would be condensed into one.

2. Improvement in staff, because of the greater attraction of the mixed work, its greater variety, its broadening effect, its more intimate relation to the whole population, rather than to the tuberculous alone.

3. Greater continuity of staff because of the greater attractiveness of the work, and therefore greater continuity of policy; better development of the work because of the greater continuity and improved quality of the staff.

4. Greater popular support because of the wider touch with the general population, and because of the broader and better results.

5. Solution of the rural infectious disease problem, including those great menaces, the venereal diseases.

6. Definite centers in rural districts for the handling of all rural health problems.

7. The securing of the great desideratum of any central government, that is, active, efficient, local centers for action.

I have so far omitted any definition of the central controlling body which is an essential to this program.

Here I confess to some doubt in my own mind as to the final solution of the question of central control, but believe that as things are now, the best control would be had by a central body, containing a representative of the state organization for supervision of state institutions, whatever that body may be called in the various states; this body to build and maintain the grounds and buildings; representatives of the state organizations on tuberculosis, whatever they may be, to deal with equipment, maintenance and staff; a representative of the board of health, to deal with the police questions that must unavoidably arise; a representative of the state educational mechanism. to deal with the school problems; a representative of the American Red Cross; a leading sociologist of the state university; and finally a representative of each county; this body to work through an executive committee, and an executive officer, whose duties shall be confined to these sanatoria.

A local county public health association should exist in every county or group of associated counties, and a committee of this county association should be the local sanatorium committee, dealing with the state central controlling body, directly or through its county representative.

ANTITUBERCULOSIS MEASURES[1]

ALLEN K. KRAUSE

Seared and battered as few other epochs of the world the twentieth century is only completing its childhood; and let us hope that its survival from maladies that only yesterday seemed mortal presages a sturdy and productive maturity and a mellow senescence. Were we required to characterize with a word the point of view,—the spirit,—that animated most of us with the birth of 1900 I believe that not a few would select "comfortable." Comfortable we were and comfortable we expected to remain. During the last two decades of the nineteenth century the conveniences of life had developed and multiplied to such an extent that what had once been the luxuries of the opulent, or had even been beyond their reach, had become everyman's necessities. And as the twentieth century added to its years, as its step became more certain and it began to reach out and grope for guidance into the mists of the illimitable future, it did so with far steadier hand perhaps than had ever drawn along any of the children of Time. For were we not at last masters of our environment? Had not the curse of our first parents lost most of its sting? Labor we must, yes,—and we must look forward ever to continue to labor. But we were to labor in a world such as our progenitors never even dreamed of. Electricity now carried us to our shops. To press a button was to light our way into our homes when we returned at night. A turn of the switch in our living room and heat began to radiate through the house. Every home boasted of arrangements that made for cleanliness, and therefore health,—arrangements that were not available for even the regents of man of fifty years ago. Almost everyone of us could sit in his easy chair and talk with his friend at the other end of the city. From our old ashes we made us dyes of a variety and beauty that far surpassed those of the plants and beetles of the sleepy Orient, and we were led to develop our taste for ornament and for clothes; and possessing more than a necessity of clothes we were led further toward cleanliness and health.

[1] An address delivered under the title, "Some Aspects of the Problem," at the general meeting of the New Jersey Joint Conference on Tuberculosis, Perth Amboy, New Jersey, November 23, 1918.

Kindred examples might be multiplied at length. But what we would emphasize is that, if the tremendous increase and widespread distribution of comforts and conveniences made for any one specific thing, they promoted leisure;—leisure, which in its enormous aggregate must have a not inconsiderable influence on the mass-manifestation of many human diseases, and particularly on such maladies that owe not a little to stress and strain to bring them to light. Among such diseases tuberculosis undoubtedly takes its place. It is not my intention to discuss this phase of the situation to-day, except perhaps to refer to it occasionally in the course of my address. But before leaving it entirely I cannot refrain from calling attention to the large part that customs and modes of life, operating over long periods, changing slowly, almost unappreciably and yet very definitely, if we consider sharply outlined economic epochs, must play in influencing the morbidity and mortality statistics of a disease like tuberculosis. It will not hamper the student of tuberculosis if he is also familiar with the history of civilization.

By 1900 we had achieved a degree of physical comfort that was before unthought of and I do not think it an exaggeration to venture that we were approaching a comparatively stable state of comfortableness in our mental concepts. In morals? Well, every age is certain of the absolute rectitude of its moral aims, even though a comparative reading of Marcus Aurelius, of Machiavelli, of Bunyan, of Pepys, and of Wesley, leaves the infant mind a bit confused. In politics? At no time were we white men more certain of our God-given function of "benevolent assimilators" than in 1900. In economics? Capital, and we are all capitalists at heart, was never surer of its complete altruism,—things moved only because we of the dollars at great sacrifice hazarded our dollars to put the wheels in motion and save those of no-dollars from starvation. In applied science? Man had embalmed the human voice to resurrect it at will. He had begun to fly in the air and to sail his craft in the depths of the ocean. He was building cloud-piercing edifices to house a small city's people in a block. He was recording actual movement and actual colors in snap-taken pictures. And so on. Man could do anything. In medicine? Deep-lying structure revealed on a photographic plate; the disabilities of the human heart transcribed in peaks and waves on a film; the provocative causes of hitherto obscure infections discovered by the dozens; totally new and unfamiliar conflicts brought to light in the humors of the body;—all these and many more achievements accumulated to convince us of our mastery over the forces of Nature and to give us a comfortable sense of security as we faced the future.

And tuberculosis? Tuberculosis also caught something of the universal and contagious complacency. Becoming enthusiastic because of several remarkable discoveries made in rapid succession we began to make claims. Made bold by unexpected successes we began to predict. We could cure tuberculosis. We knew its cause—the tubercle bacillus. We were also sure of how the tubercle bacillus came to us. We could, therefore, choke it off at the source and prevent tuberculosis. Indeed, so flushed were we in the first days of our new knowledge that we set the date for the disappearance of tuberculosis, and few of us are so young that we cannot remember the banners that flaunted, "No tuberculosis by 1915!" Unmindful of the many disappointments of the past, careless of the one outstanding fact that is so familiar to the student of tuberculosis, namely, that almost every new discovery, almost every penetrating ray of light, once its full significance was appreciated, had never failed to indicate how much more complex was our problem than we had imagined, we pressed boldly on and made up our antituberculosis program.

This program was simple and it was direct. Based on the several plain facts that I have just outlined it was thoroughly logical and understandable. It is familiar to you all and may be summed up in a few words: institutions for the sick, the detection of disease at its very beginning, and the control of the sources of infection.

Has it worked? I am told almost daily that it has not. But I always feel that the man who asserts that it has been a total failure and that it has contributed nothing to the salvation of the race is speaking altogether outside the facts. I know many men alive and highly productive to-day, who had the good fortune to become consumptive in the early nineteen-hundreds rather than in the eighteen-seventies. Thirty years before they would have been doomed to death and most of them would have died. I also know many "trained" consumptives who have fought their disease to a successful issue, and who have done this with their healthy babies around them, yet who fifty years ago would have sent many of these babies to scrofulosis and to death, and passed the blame therefor to their inherited taint. There can be no doubt that our program of control and our vulgarization of information have saved countless human lives and have prolonged ten times more. They have thus contributed tremendously to the potential and actual wealth of the world and have just as surely paid back to the people every penny they have ever received from them. A week's "sociological" inquiry will

convince any unprejudiced person of these facts and should be sufficient to silence any destructive critic of the organized antituberculosis movement. But criticism there will remain and criticism there must remain if our work is to keep from stagnating and if our methods are to be kept so elastic that they can take advantage of the newer concepts that fresh contributions to knowledge are continually introducing.

Thoroughly convinced that the organized antituberculosis movement has exerted a tremendously salutary effect and just as certain that every man who is interested in any way whatever in the conquest of tuberculosis should wholeheartedly and unselfishly work toward a common end through one organized body, I nevertheless do not consider it conclusively proved that our organizations have always made full use of the more advanced knowledge of the day or that they have adopted all this newer information to themselves and applied it in all its implications and ramifications, no matter where these led. A certain fixity and non-development of the original plans, first bruited about the beginning of the century, have more than once impressed me. These plans, as I have said, were comparatively simple and direct. Few will disagree that they laid an overwhelming emphasis on the dangers of infection and on the necessity of paying attention to the sources of infection. In other words, they only followed the leading thought of the day, which was the outgrowth of the tremendous bacteriological bias that Koch and his followers saddled upon preventive medicine. They were formulated at a time when common opinion held that tuberculous infection and manifest tuberculosis in an adult were almost simultaneous occurrences. And if this appreciation of the tuberculosis situation had been a true one I believe that as a public health body our National Tuberculosis Association would have made far more progress in combating the disease than the steady strides it has already taken against a problem of almost incredible difficulty.

Our awakening began almost so gently that most of us refused to be stirred up. We may date the dawn of this new day to the Pirquet test. This simple manoeuvre, innocently put forward to aid us in diagnosis, to detect the consumptive even before he is aware of impending trouble, did not fulfill its original purpose. It did not point out who were tuberculous enough to be treated and who were not; and viewed from this angle it was a failure and exhibited a striking parallel to the fate of Koch's original attempts at the prevention and cure of tuberculosis. But never did a failure lead to more significant results! After several

years,—after much grist had gone through the mill, it was found that the Pirquet test and all that it may mean had taught us many things that most of us would not have believed a decade before. Indeed, so multiform and far-reaching are its implications that it is my own opinion that with Laennec's promulgation of the unity of phthisis, Villemin's discovery of the infectiousness of tubercle and Koch's revelation of the bacillus, it makes up *the* quartet of really great episodes in the history of tuberculosis. And in some respects I consider the era of ideas,—ideas, many of which are still relatively embryonic and formless,—that it ushered in as the greatest of all.

It made absolutely certain what a very few sturdy souls had previously suggested and what still fewer admitted, namely, that the generality of mankind that lives in close association with its fellows harbors the tubercle bacillus; that is, that most of us become infected comparatively early in life. Try to think now of all the implications that this one bare fact conveys. What a vista of the ubiquity of the tubercle bacillus it at once opens up,—a ubiquity such as even the early bacillus hunters from Koch to Flügge never even dreamed of! Where then shall we begin in our search and control of sources of infection? Why, with the man of "positive" sputum, of course. Granted;—and that too would be relatively easy; but where shall we go next? Why, to the manifestly ill who may not be emitting bacilli. Let us go even further and refine our diagnostic methods and attempt to ferret out those who are not yet ill but who are about to become ill. We won't quarrel over whether this is possible or not: we shall set out to do it. Yes, and where then?—for we have thus far accounted for only the veriest fraction of the human race that is carrying around tubercle bacilli.

But,—you protest,—what difference does it make if nine-tenths of the harborers of tubercle bacilli, all healthy men, do carry with them the seeds of consumption? They are "safe" men. They are well and are not distributing bacilli among their neighbors.

Yes, they are "safe." But they are "safe" only so long as they are "safe" and who is there anywhere so endowed that he can detect the moment, the day, the month, aye, in some cases the year, that they pass from being "safe" neighbors to a menace? And in this period of dawning disease, this indefinite time of diagnostic uncertainty before the patient seeks medical advice, how many cycles of infection, think you, can the patient initiate? It has always been my impression that by the time a very average and a very large number of us come to our

physician because of our tired feeling, or our cough, or our lack of endurance, we have already fairly thoroughly tuberculized most of those who move within our range of intimate contact.

The Pirquet test gives us a method to make epidemiological studies such as is possessed by the students of no other disease. Equipped with it and its modifications we can roam the world and make observations on man and animals everywhere and, with an error that is surely less than ten per cent, detect who is tuberculous and who is not. And when we observe infection among the very young, whose voluntary range of contact is quite limited, we should more than once be led to the detection of previously unsuspected sources. Epidemiological studies have been made, but all have been too limited and too sporadic. And we await the day when the state, or men of vision and large resources, shall make it possible for us to have ideas that are definite and well grounded because they are based on sufficiently broad observations. It has just taken billions to still the voice of autocracy and brutishness, and mankind has gladly given up its billions. Yet the voice of Benedict Spinoza, that "God-intoxicated man," was stilled by the tubercle bacillus, and we go stumbling along in our search for truth for want of the thousands to lay bare the tricks of the eternal enemy of all mankind.

How significant becomes what the Pirquet test now teaches us! If most of us harbor the tubercle bacillus and if at the same time but a small percentage of us ever falls sick with tuberculosis then nothing can be more certain than that the development of manifest disease, the efflorescence of a "safe" man into a menace, depends not so much upon the mere presence in us of the seed,—in other words, upon infection,—as upon some other factor or factors that enter into our experience. Not all these factors are by any means familiar to us: indeed, we probably are acquainted with very few of them specifically. But I do not think that we generalize too rashly, if we are not too "scientific" to refuse to learn from clinical experience and say that a large proportion of the outbreaks of manifest tuberculosis are attributable to non-specific bodily effects that are brought about by what we may in general call "strain." Here we might classify the circulatory changes that are set up around old, unknown, and quiescent foci by such events as pregnancy and labor, intercurrent disease, sudden intense or prolonged and more moderate physical effort, emotions such as anger or worry, abnormal habits or dissipation. Though its *modus operandi* is disputed, most men to-day agree that strain is an all-important factor in bringing tuberculosis into

the realm of consciousness; and, if this be granted, it must be equally true that its opposite, that is, relief, or comparative relief, from strain will operate toward keeping quiescent tubercle in abeyance. It must therefore be perfectly certain that anything that leads to an amelioration of the general habits and conditions of life of masses or classes of people will work toward a subsidence of tuberculosis, epidemiologically speaking. And you will at once catch the drift of my remarks at the opening of this address, that in appreciating the significance of the ups and downs of tuberculosis as a folk-disease we must also have some comprehension of the civilization of a people at any particular period that may be under consideration.

Our statistics, particularly those of the earlier decades, are anything but satisfactory and complete. Nevertheless they bring out one thing clearly. This is, that the tuberculosis mortality rate began to decline in practically every country that was advancing industrially and was therefore increasing in wealth, as early as 1850 and for perhaps ten or twenty years before. This, remember, was thirty years before the discovery of the bacillus and when the disease was universally regarded as having a diathetic basis. In other words, tuberculosis began to abate its terrors before man intentionally applied a single measure to combat it. This fact must be familiar to you all and I shall not go into further detail concerning it. Personally, I can see only one reason for it, and this is the gradual bettering of the conditions of labor and living of the mass of the people that was ushered in markedly shortly before the middle of the last century and took on a tremendously accelerated impetus after 1880 and proceeded at an ever-progressing rate with only one or two brief interruptions (from 1893 to 1897 and in 1907) until the release of Armageddon in 1914.

Public health men have on occasion not been slow to seize upon this phenomenon and to throw it into the teeth of our antituberculosis boosters and boasters that figures showed that our own efforts had contributed nothing to a lessening of the greatest of all plagues but that this was brought about by forces that were intangible and over which we had no control. But truth is, that to speak thus is to argue, let us not say unfairly, yet nevertheless on a pinpoint. Such an assertion can be made to return like a boomerang upon the declarant. And, if we wished to draw comparisons and take a broader stand on the matter of infectious diseases in general, then following out the same line of argument, we should come dangerously close to a negation of the effect of public health work in general.

If we examine vital statistics we find that of the infectious diseases a decline in the death rate that began before what we may call the bacteriological era was not confined to tuberculosis alone. This is true of a number of diseases that we may call endemic in this part of the world, —of scarlet fever, of measles, of whooping cough, and of the enteric infections. We do not know the provocative causes of scarlet fever and measles, and cannot therefore combat them by specific measures. Yet scarlet fever has shown a marked decline, both in incidence and malignity, since about 1870. It must be obvious that as the habits and modes of living of a population change there must be many balancing and opposing forces set in motion which make both for and against the occurrence of infectious diseases. On the one hand we should expect that the enormously accelerated condensation of population and the unexampled development of the means of communication that have been going on in the United States during the last thirty years would, if they were unopposed by contrary factors, favor the spread of many infections. But against such forces we may put the high development of home and office and factory sanitation, the better and more equable house heating brought about by central heating systems, the tremendously increased interest in out-door play and sports, the reduction of the hours of labor, the more general enjoyment of vacations,—in short, anything and everything that contributes to the amelioration of social and domestic life.

We now take our enormous office buildings as a matter of course. We have seen architects erect the impossible and we have long passed the time when anything that is built can elicit an expression of amazement from us. Yet we seldom stop to think that even though we were in possession of all the secrets of the assembling of structural steel and even though we could install our present-day elevators, it would be absolutely impossible to use these great buildings, to bring together myriads upon myriads of people on the ground-space of an acre, if we could give them no better sanitary appliances than those that were in vogue as recently as thirty years ago. Our great buildings depend just as much for their erection on latter-day plumbing as they do upon the development of the elevator and the structural steel industry. And when we assemble people together as we do to-day, we are doing this under conditions that, as regards many infectious diseases, are relatively healthful compared with those that obtained only a few decades ago; and these physical conditions originated not in the minds of sani-

tarians and public health officials, but in that greatest of all stimuli for the betterment of man,—industrial ambition in its quest for wealth.

It must also be self-evident that as a community like that of Manhattan Island, in its necessity for growth and expansion, reclaimed and built up the vacant stretches and waste areas of land and erected buildings upon these, it unconsciously, with no thought whatever of public hygiene, brought about conditions that were unfavorable to the development of several infections. Malaria would be one of these; endemic typhoid fever another. We might go on and develop this phase of the subject indefinitely. But I have already taken up perhaps too much of your time with it; and I have brought it in to illustrate that not all betterment of health conditions need be due to the intentional efforts of sanitarians, and to give point to what I feel, namely, that the public health official and "scientific" investigator, who now and again calls upon us to demonstrate mathematically the net results of our efforts and who seems inclined to dislocate credit from us to other broad and more or less intangible forces, had better analyze honestly just how many endemic infections he has *by intentional intervention and by this alone*, diminished or subdued.

I am conscious of the enormous part that public health has played in making our residence on earth livable. As an outsider, I have always been proud of what our more enlightened and untrammelled executives have sought to do and have actually accomplished. But I also feel very strongly that as a body and as an arm of the public health service, our own National Association has never stood second to any in tangible results, that it has had as much definite information at its command as is at hand to combat any contact infection, that in the main it has used this well, and that because of its personnel it is unique and works with far more "motive" than any other aggregation of public servants in the world. For remember, the vast number of us are those who, having tasted, having felt, and having gained a personal and individual victory, have now enlisted in the most disinterested service. There are few of us who are in this fight for gain; still fewer for fame. But most of us work on because we have been taught by a great disciplinarian and because we would render back some of our mortal hours to the cause that gave them to us. And lest you think that I have now struck the level of sentimentality and that I am indulging more in oratory and in poetry than in fact, let me say that not so many years ago I expostulated with some heat with a man who has stood as high as

any in our antituberculosis movement. I tried to point out to him that it was time wasted to spend so much of his precarious strength in public addresses and organized efforts to fight tuberculosis. And he replied that the movement initiated by Dr. Trudeau had given him back his life, that he owed everything he was and had to tuberculosis, and that the least he could do in return was to give up to it every minute he could spare. These were the words of a "lunger." And there are many others like him.

To come back to the disclosures of the Pirquet test. Let us ask how these square with the basic measures of prevention and control as these are embodied in our present program. Let us also seek to discover whether they teach us anything of value that might profitably be employed to supplement our orthodox efforts. But let us first run over briefly the chief weapons of defense that we now employ.

The institutional care of the tuberculous sick has proved its worth and has come to stay. It is yearly rescuing thousands of souls from an early grave or adding to their years. Fundamentally the principles that gave it birth are sound and will withstand any amount of shallow criticism. It has never yet been given a complete test for the simple reason that no community has as yet seen fit to appropriate enough money to take care of every one of its tuberculous patients for a proper length of time. But even though this could be done throughout the entire nation, there is not the shadow of a doubt that institutional care *of itself* would not solve the tuberculosis problem. It would not solve it because infections would still be taking place,—infections that planted the seeds of potential consumption. And infections would continue to take place because it is unthinkable that more than a moiety of patients would be detected before they had reached the "bacillary" stage, clinically speaking. Therefore, before entering sanatoria a large number will have tuberculized many with whom they live and associate. Properly speaking, institutions for the care of the tuberculous have but small place among the measures of prevention and control. They furnish abodes for reconstruction, education and rehabilitation, and should be looked upon as such. From the point of view of preventive medicine the greatest argument that can be brought forward for them is one of reasoning by analogy,—of comparing them with the lazar-houses that so successfully combated leprosy during the middle ages. But the analogy is not quite apt for reasons that would take us too far afield to discuss. We will here content ourselves with pointing out merely the

differences of infectiousness between the two diseases, the differences in onset, and the differences in termination between two diseases, one of which goes on inevitably and in the main progressively to death while the other is eminently a disease of "self-arresting" periods intermingled with relapses, progressions, and retrogressions, that no man can accurately predict, and not too many appreciate.

Even though it could be shown that, under certain happy hypothetical conditions that so far as I know have no counterpart on earth, the incarceration of all consumptives would be eminently a preventive measure rather than one of reconstruction, its complete success would be of necessity absolutely dependent upon making a diagnosis in every case of tuberculosis in a stage that precedes the emission of bacilli. This I do not consider even quarter-way possible or practicable. After reading certain discourses on early diagnosis one would get the impression that the ordinary case of tuberculosis originates with the definiteness and abruptness of measles or the semi-obtrusiveness of typhoid fever. But I am confident that there is not a clinician here who will not agree with me that if there is any one feature that only too commonly characterizes the onset of tuberculosis it is that it comes on in such a way that for a considerable time the patient has not the least idea that he is an ill man. He has symptoms, it is true; but what are they? Only too often the same slight disabilities that he has frequently suffered before, and which he more than once shook off. A normal man, unaccustomed to introspection, to hypochondriasis, and to unnecessary self-worry, will not run to a physician because of the slightest indefinite pain or lapse from full efficiency that oppresses him, and it is notorious how often we encounter these symptoms in people in whom we can find no organic basis for their complaints. It is just as notorious how often vague, indefinite and masked symptoms,—deviations from health that do not seriously interfere with a man's pursuit of his occupation,—usher in the full expression of tuberculosis. And it is no less notorious how far a tuberculous process may progress anatomically before it addresses itself more eloquently to the patient. All this is so well recognized that I would hesitate to hazard even a guess as to the mean length of time that elapses between the first manifestation of illness and the seeking of medical advice in the ordinary patient who begins his tuberculosis career as a case of chronic or indefinite onset. I only know this,—that I have seen a prominent pediatrician present himself to the phthisiologist for the first time twelve years after his cough had begun. And he arrived with both

lungs "riddled" and sputum loaded with bacilli. I have seen an eminent judge first ask for advice thirty-five years after his disease had given out its first warnings. And he came with cavitation in both lungs and a sputum count that would have caused Gaffky to create a new classification: yet he was a supreme court justice and had lost but few days of a busy lifetime from his labors. I also know of a pathologist who for eight years had the symptoms that we classify under the cardio-gastric type of onset, who at last had râles that came and went, and who finally went on to bilateral disease; yet although under constant observation by the best men he was not declared tuberculous until bacilli appeared in his sputum after nine years. The day of his first manifestation of bacilli must of course forever remain unknown, as must the damage that he did between the first "show" of bacilli and the time of their detection.

These cannot be exceptional instances. And they must make us wonder, that if such things are so, what then is going on among the more uninformed. We can only speculate: and I do not believe that the most florid imagination will over-daub the canvas. But if a large number of patients will not seek medical advice until some time after the first manifestation of symptoms, and if the diagnosis of pulmonary tuberculosis can offer insuperable difficulties to the best physicians,—and I do consider that both these provisos are actualities that complicate the tuberculosis situation,—then, it is manifest, that even though every medical man in the world possessed a degree of diagnostic skill that is at present unimaginable, there would still be ample opportunity left for a fair saturation of the world and the people who live therein with tubercle bacilli. And this statement of necessity carries with it the corollary that, as a measure of control and prevention, early diagnosis must ever be a limping sister.

No, to be *of itself* an adequate preventive method we should have to imagine that the following grotesque approach were workable, namely, that every man, woman and child submit, not monthly, but weekly or even daily, to physical examination and questioning by a competent clinician,—by one who has "tuberculosis judgment." I say not monthly but weekly or even daily, because tubercle bacilli that have been turned loose can get to many harbors in the space of a month. I use the term "competent" advisedly, for reasons that must be apparent to all of you.

Whenever I think of early diagnosis, I think of it, not as a preventive measure essentially or as one of control, but, like institutional care, a

salutary measure. And I am never tired of emphasizing that the more physicians there are or will come after us, who from a proper adjudication of history, symptoms, and signs can arrive at an appreciation of the earliest manifestations of clinical tuberculosis, the more human beings there will be who will be snatched from the ravages of the tubercle bacillus. It will reduce somewhat the chances of infecting others, but, if we honestly face all angles of the situation, the rôle it can play in limiting infection must be as a drop in the bucket. Nevertheless, because it is a life saver, it must ever remain the keystone of the clinical arch of tuberculosis.

We come now to the matter of infection. And here I must pray that I be not misunderstood.

As nearly as I can determine infection is the shibboleth of the antituberculosis campaign. Now and then I go to a tuberculosis exhibit. And what do I see? I see posters everywhere, portraying what we must avoid in this everyday life of ours if we are not to gather to ourselves the tubercle bacillus. I see very visible sneezes and coughs projected toward innocent bystanders. I see clouds of dust cast up by the sweeping broom to the nostrils of anyone who happens to be in the way. I see Susie using Johnny's tooth-brush. I see a pale, though heartless, mother imprint the kiss of instinct upon her baby's lips. All this and much more. And the implication is always plain. This dust, this mouth spray, this vicarious tooth-brush, this kiss, is the cause of consumption.

But is it?

I shall answer by saying that I don't believe it is. It may propel into us the tubercle bacillus. It may even start the anatomical reaction of tubercle. But the number of times that it goes straight on to consumption is negligible,—so negligible that I don't think that we need concern ourselves about it.

Why should we concern ourselves about the *mere presence* of tubercle bacilli in our bodies? The Pirquet test has taught us that all who have taken their place in normal social intercourse have it attached to them. Yet the workers of the world go on, creating and undoing, and amassing and dissipating, all infected, yet few invalided. Considered by itself, therefore, mere infection is hardly worth paying attention to. It is the normal lot of man. The pessimist, upon first hearing of the universality of tuberculous infection, will throw up his hands and exclaim, "What's the use." The optimist will throw up his hat, and declare, "It can't be so bad after all. Everyone has it, yet few are sick."

We should take a far firmer hold on this fact than we have done heretofore. We should spread it broadcast. We should drive it home to every man that before adolescence tubercle is more common than hair on the face, and after forty, more common than hair on the head; and in a great proportion of instances not so troublesome, unless he makes it so. In 1900 it was infection that we were interested in; and naturally so, for it then meant disease. But to-day it is again consumption and its prevention that are our province, for we have learned of how little moment mere infection really is.

I have thus far not dwelt upon one phase of the antituberculous movement that organized effort has always made more than one-half of its program, and which must ever remain its chief function. This is education, so called.

But what is education? Whom shall we educate? And what information shall we impart?

In propagandism we speak much of education. Only too often we seem to imagine that its beginning and end are the dissemination of information. Yet real education is vastly more than this. To scatter broadcast and aimlessly what he knows is wasted time for any teacher. The process of education presupposes that besides being given our information is received, understood and assimilated. Only too often we teachers cast our pearls before swine. . Only too often, too, we consider our function fulfilled when we have thus delivered ourselves of a weighty homily. And much of the education of health associations has, to my way of thinking, often proceeded in this haphazard fashion. Therefore, when I am told that to-day the people and the medical profession are already "educated' as regards tuberculosis, I react with a gesture of scepticism and unbelief. That tons of literature have been scattered to the four corners I do not doubt. But that pounds of what is really worth while have sunk in I do doubt.

The remedy? Why, teachers: teachers who can make their point, who can inspire and who can direct. If it be desirable to instruct youth how to take its place in the world and make its living, how much more important is it that it be taught how to preserve its life! Under the patronage of the state a highly organized body of unselfish men and women are preparing our sons and daughters for the duties of life. And had I my way I would see to it that we of the National Association would select a great corps of the most elect of mankind, of teachers, and send these out to tell their fellowmen how they

may preserve their lives. I should attempt to have these teachers trained in all the essential particularities of tuberculosis and of public health. I should send them to the people and I should send them to the physicians. And what would I have these told?

Much more than I can here take up to-night. But I would have emphasized that tuberculosis, a gaunt, manifest upheaval of pulmonary infection, has its birth, not so much, if you please, in an ertswhile localization of the tubercle bacillus, but in any and every event that makes man unhealthy. I would have them told that to be spat upon or coughed upon by the man with the "common cold" did not upset me because I might merely acquire a cold quite so much as that this cold might fan my quiescent pulmonary tubercle into phthisis. I would have them told that the delicate woman who was about to fulfill her grandest function should be handled just a little differently from the sturdy one,—that her labor should be shortened, that her lactation be directed with the possibility of manifest tuberculosis ever kept in mind. I would have them told that over-strain, whether physical or mental, or that dissipation was to be avoided, not *because it laid them open to infection, but because it supplied the oil to a wick that was already present. I would have the emphasis laid on the behavior of the human being and not on the bacillus.* And I should thereby be contributing not only to a solution of the tuberculosis problem, according to the best information available, but also to that larger problem, that of public health in general.

After all, there are only two conceivable short cuts to the eradication of tuberculosis.

The first is the universal use of a remedial agent that would cure any and every type of disease without harm to the patient. We would presume that such a preparation would be bacillicidal. If it was capable of curing every case of manifest disease and could at the same time sterilize all tissues we would presuppose further that it could free from bacilli all foci that lay concealed in those without manifest disease. If, therefore, we were in possession of such a potent medicine, we could at any given time, by edict or by common agreement, administer it to all people and to all animals that are susceptible to the tubercle bacillus and at one grand stroke wipe out all tubercle bacilli that were in parasitic association with tissues. And this would undoubtedly mean the end of tuberculosis on earth.

The second short cut would be to administer to every non-tuberculous individual and to every new-born susceptible animal over a period of

several generations a something that would immunize them in a way that they would be secure from any tubercle bacilli that attempted to gain lodgment in their bodies. This, manifestly, would be a more leisurely method than the first; for with only this weapon in our armamentarium, before the bacillus disappeared, we should be obliged to wait until the present myriads of victims,—our phthisical grandfathers and our tuberculous children as well,—squared accounts with their unwilling and ungrateful guests,—obligations of a kind that are never adjusted with finality till Death, the only non-appellate arbiter, comes between. The more halting of the two, this procedure would, none the less, also spell the end of tuberculosis.

Neither of these short cuts is in sight, nor can our generation hope to take the journey. Meanwhile I would stress that the prevention of tuberculosis is a prevention, not of infection, but of manifest disease; and that all our efforts should be directed to a supplementary reëducation of physician and layman alike, and to the study of every factor that makes infection disease. And at the risk of unnecessary repetition I would also point out anew that there is no one shining beacon to lead us to the control and prevention of tuberculosis. The very complexity of the situation forbids this. I would not abate one jot or tittle of any tested method that we have employed. But I would take advantage of what the last decade has brought to us and lay the onus on the human individual rather than on the infecting microörganism.

The opportunity for service in antituberculosis work is tremendous: so tremendous as to appal the individual who for the first time casts his eye over the fields to be made over and the roads to be travelled. The opportunities for philanthropy are no less great and in no human endeavor will money spent yield more certain and richer returns. We must have a goal and this goal must be the complete taking-over of the tuberculosis situation throughout the world. We must cry for money and money and still more money, and never cease until the mass of mankind realizes the situation and is responding to it. Then and then only can we say that we are in a position to wage a real battle against tuberculosis. An effective fight would presuppose an organization the spirit and model of which could be found only in the monastic orders of medieval times. Our sisterhood, made of up thousands who have given back their lives to tuberculosis, would live among the sick and bring them back to a measure of effectiveness. Our friars would go up and down the land instilling the people with the truth,—the truth

of the universality of the tubercle bacillus, the truth of the magnitude of its mortal effect, the truth of the inciters of the tubercle bacillus to action, the truth that everything that makes for the internment of the tubercle bacillus within ourselves makes for better living and higher efficiency and that everything that makes for better living and higher efficiency makes for the internment of the tubercle bacillus. Without rest, without interruption or let-up, we must keep all this before the people, while our priors and our abbots are busy in recording the peculiar habits and characteristics of the enemy and the responses and reactions of the body to it. Acquisition of all information, broadening, intensification, growth, and development, must never cease in our plans of campaign. Apologetic we need not be and dare not be; and no real worker should be obliged to approach the shrine of wealth with hat in hand to ask for a pittance for the cause. It is the glory of mankind that it has always been responsive to necessity; and real information that brings about an adequate appreciation of the necessities of the situation will always loose the purse-strings.

Nor is there room in the antituberculosis movement for a single note of discouragement. The pessimists among us can be only those who are deficient in grasp and breadth. Civilization and tuberculosis are cotemporaneous; the number of the tuberculous and the number of civilized beings are almost coequal: therefore, to despair of tuberculosis is to despair of civilization. A graft that is as much a part of us as the development of our ethical sense cannot be lopped off in a day; but it can be kept from flowering and bearing fruit. And until we can wage direct warfare on the germ, to keep it in the seed should be our main purpose.

MEDICAL NOTES, ABSTRACTS AND REVIEWS

It will be the eventual purpose of the REVIEW thoroughly to canvass all literature on tuberculosis as it appears in other medical periodicals and to present it in abstract form. Authors are requested to send abstracts or reprints of their papers to the Abstract Editor, Dr. George Mannheimer, 41 West 51st Street, New York, N. Y.

Cyanocuprol.—About 200 patients have been treated with Koga's cyanocuprol from May, 1915, to the end of that year. Thirty-eight were in the first, 93 in the second and 52 in the third stage. There were two series of cases treated, one at Tenneji and one at Hamadera. The results differ somewhat in the two localities, probably because at Hamadera the patients come from a class living under better social and economic conditions, and because of other differences in the hygienic and dietetic treatment, which are of importance in the treatment with cyanocuprol as in any other treatment. The percentage of cure for first stage cases in Tennoji and Hamadera were respectively: 58.8 and 76.4; for second stage, 25.0 and 15.8; for third stage, no cures reported. The following percentages were "much improved:" first stage, 35.3 and 19.1; second stage, 55.5 and 49.1; third stage, 41.2 and 33.7. Between 1 and 2 per cent were reported worse; the remaining cases were somewhat improved or not improved. The patients should be treated in hospitals only, as many accidents may occur in ambulant cases, especially when there is a tendency to hemoptysis. If there is suspicion of intestinal tuberculosis the bowels should be thoroughly evacuated before administering the drug. Twenty-four hours of absolute rest after the injection are required, after which the patient may sit up for the following forty-eight hours. A half fluid diet is given. Smaller doses than those given by Koga were found necessary. In first stage cases, 5 to 6.5 cc.; second stage, 3 to 4 cc.; third stage, 2 to 3 cc. Where there is a history of hemoptysis smaller doses are given and the succeeding dose is regulated according to the observed effects. Success depends upon the proper dose for each individual case, the effect bearing resemblance in this respect to tuberculin. Cases of acute pleuritis were not treated, and in chronic pleuritis little effect was noticed. In intestinal tuberculosis special attention must be given to evacuation of the bowels and to diet as the injection is often followed by pain, bleeding and fullness. In early glandular tuberculosis the remedy is sometimes wonderful in its results after several injections, but a somewhat larger dose is indicated in these cases. In laryngeal tuberculosis the effects are not marked. The reactions following the injection are both general and local. In afebrile cases a suitable dose usually does not cause a febrile reaction. Where there had been some fever a rise follows the injection which subsides within one or two days. The reactions are less marked after subsequent injections and ultimately disappear altogether. The pulse is often slowed down, but this effect is no doubt due, in part at least, to the rest in bed. The initial tendency to increased perspiration (about 50 per cent of cases) lessens and disappears after several injections. In rare cases the following ill-effects follow administration of the drug: headache, slight fever and flushing of the face; oppressive feeling in the chest, discomfort in the stomach and intestines. These pass off within two or three days, and may be avoided by giving a smaller dose. There is often also an initial loss of weight, increase in cough and expectoration coming on one day after the injection, loss of appetite. increase in the number of tubercle bacilli hemoptysis, and aggravation of the physical signs. All these become less pronounced after subsequent injections until they disappear entirely. The remedy is contraindicated in advanced pulmonary tuberculosis, in highly febrile cases, in general miliary tuberculosis, tuberculous meningitis, recent pleurisy or peritonitis, and advanced intestinal or laryngeal tuberculosis. It was found that injecting 5 to 10 cc. of a 5 per cent solution of calcium chloride with the cyanocuprol preparation will often prevent the untoward effects mentioned, especially hemoptysis. It is essential to combine cyanocuprol with sanatorium regime. If the patient is not improved, or is weakened, after two or three injections the dosage should be re-

duced or the interval extended. If this brings no improvement the treatment must be given up. Even when the treatment brings improvement after each injection, the treatment is best interrupted between the fifth and sixth and between the eleventh and twelfth injections, for at these times the improvement is most marked, and continuation of the treatment may cause harm. If the individualization, which is especially important with this remedy, is properly carried out its value is indeed remarkable, surpassing all other remedies ever tried. The addition of calcium is beneficial and does not alter the efficacy of the drug.—*Clinical Experience with Koga's Cyanocuprol., T. I. Masuda and T. K. Matsuda, Am. J. M. Sc., July 1918; clvi, No. 1, 78.*

Management of Renal Tuberculosis.—Bugbee summarizes the present status of renal tuberculosis as follows: Renal tuberculosis may be a primary lesion and arise from a filtration of tubercle bacilli from the blood stream into the parenchyma of the kidney, where tissue changes similar to those found in tuberculous foci in other parts of the body take place. An effort is always made to wall off the process but the formation of antibodies is so slow, and the immunity of the patient, which may have been always absent or which may have been temporarily diminished, is so low that the lesion usually gets beyond control, and usually goes on to wide destruction of the kidney and extension to the other kidney, to other parts of the urinary tract and of the body. From the nature of the lesion remissions are common. The symptoms of renal tuberculosis are misleading, often slight at the onset, and give no indication of the extent of the lesion. The diagnosis of renal tuberculosis may be simple or the most difficult of all urinary lesions, often requiring preliminary treatment to allay acute symptoms and repeated cystoscopic examinations over a long period of time. The treatment cannot be outlined from a study of the symptoms. The remission of symptoms, often for long periods of time, should not be accepted as a cure. The effort on the part of nature to inhibit the progress of the disease and to limit the lesion should be borne in mind, utilized and encouraged in every possible manner in inoperable cases, before as well as after operation. While the review shows that many others have had cases similar to two quoted by him, where the active tuberculous process has been arrested and walled off, still this is not the rule, the lesion being progressive. Even when arrested, a kidney the site of poorly drained cavities is a menace to the system. Therefore, nephrectomy is the proper treatment. With the means at hand by which we can often make an early and accurate diagnosis of renal tuberculosis, and with our statistics showing that seventy-five per cent of the cases of unilateral infections are cured by nephrectomy, the tendency is to be too optimistic as to the future in these cases. They should all report regularly, be watched and treated as cases of general tuberculosis.—*Management of Renal Tuberculosis; Report of Cases, H. Bugbee, Surg., Gyn. and Obst., May 1918, xxvi, No. 5.*

Significance of the Cuti-reaction after Tuberculin Inoculation.—Lanz sums up his extensive study as follows: Repeated cutaneous inoculation with tuberculin exert—like the injections of the same—a curative effect, the tuberculin being built down to harmless substances, protective antibodies are formed, the system is detoxicated. These processes come about through reactive inflammations in the superficies of the skin as a result of which diseased foci are spared and an injurious general reaction is avoided. Hence cutaneous reactions are superior to injections for the latter are associated with a hemic reaction. Sahli's procedure with groups of punctures is superior to others provided the dosage and increase are proper, because the conditions favor a larger dose of tuberculin. The cutaneous method is readily carried out in the case of the curative and symptomatic treatment of mild and severe cases respectively and is also adapted to the prophylactic treatment of those who have been exposed or who have latent foci. Hence it is possible to use it in the group treatment of the public under certain conditions. The services of several practitioners may be necessary and the group should be treated over a considerable interval. The dietetic-hygienic treatment should be maintained with its customary rigor.—*Ueber die Bedeutung der Haut-Reaktionen nach Tuberkulin-Impfungen zur Therapie and Prophylaxie der Tuberkulose, Lanz, Corr. Bl. f. Schweiz. Aerzte, July 27, 1917, xlvii, No. 29, 920.*

Death Rate from Tuberculosis in the Principal Cities of the United States.—According to a bulletin published by the Health Department of Chicago, among the ten principal cities of the United States Pittsburgh has the lowest death rate from tuberculosis, for the year 1917, the rate being 147.05 per 100,000 population. Chi-

cago is a close second with a rate of 148.67 per 100,000. The rates of other cities in this group are: Detroit, 160.66; Boston, 170.87; Cleveland, 174.7; New York, 176.75; Philadelphia, 194.81; Los Angeles, 199.42; St. Louis, 202.95, and Baltimore, 236.61.—*Bull. Chicago School of Sanit Instruction, April 27, 1918, No. 17, 67.*

Regulation of Dispensary Treatment of Tuberculosis.—The New York City Department of Health has adopted an amendment to the sanitary code which provides that "no public dispensary where communicable diseases are treated or diagnosed shall be conducted otherwise than in accordance with the regulations adopted, which are to take effect at once." These regulations require that examination and treatment of persons affected with tuberculosis shall be conducted in a special dispensary or department maintained solely for such purpose; that every dispensary be provided with adequate facilities for making microscopic examinations of sputum; that the number of patients examined by one physician shall not exceed five per hour; that every dispensary shall be open at least one day each week for the reception and proper care of patients, and the necessary medical and nursing staff shall be on duty on all the days set apart for the reception of patients; that an adequate follow-up system be maintained; that circulars of instruction and advice be furnished patient; that every dispensary shall examine, and, if necessary, treat at the time of their first visit, all applicants, irrespective of their place of residence; that a complete and adequate record be kept of every case, and that such records shall not be open to inspection by the public or to any person other than the representatives of the Department of Health and such persons as may be authorized by law to inspect such records; that every dispensary in which persons are treated for tuberculosis shall be provided with and employ proper facilities for the examination and treatment of the nose and throat of such patients.

Community Organization.—A thorough piece of organization for the purpose of educating the public in the different phases of anti-tuberculosis work will use every available grouping of society, every agency, every line and channel in spreading the gospel. There will be found a distinct channel for every group of individuals. In Framingham, an outline questionnaire was prepared, called "Know Your Own Town." It was divided into chapters dealing with the history, government and finance, housing, health, recreation, industry, immigrants, child welfare, delinquency, charities and organizations of the town. This was turned over to the principal of the high school, who, in turn, divided it among the various classes according to their particular study. Thus, to the class in Science was given the chapter dealing with the question of health. The teaching of simple good health and hygienic habits to children is one of the most vital things in all anti-tuberculosis work. The child agrees to do eight health chores every day. They are such simple things as: brushing his teeth, drinking so many glasses of water, washing his hands before each meal, sleeping a certain number of hours, and keeping his bedroom window open. He is given credits on his score card for every chore he performs, and there are honors in titles and pins, which act as incentives. The Framingham experience is that continuous publicity, through the clubs and lodges, the newspapers, the churches and the factories, is the policy to be pursued. Every club and organization should have a member appointed regularly to give the news at their meetings. Posters are ready for distribution to the factories. Ten of these will be issued serially, each one carrying some eye-arresting phrase. The theatres and moving picture houses should also be utilized as very potent factors in educational work.—*Adequate Community Organization for Health Educational Work, M. A Abel, Boston M. and S. J., June 20, 1918,; clxxviii, No. 850.*

Activities of Massachusetts League.—During the year almost 27,000 pieces of literature were distributed. A new leaflet, "Facts for Fighters," comprised the largest number and was sent to the various local boards and cantonments. Six educational articles on tuberculosis were purchased and are to be used as copy by the pupils in stenography schools. Over 6000 press bulletins from the N. T. A. were sent to city and state newspapers. A series of lectures was given to the medical officers at Camp Devens. The most important measure affecting tuberculosis was one passed by the 1917 Legislature, allowing the State Board of Charity to pay ten and one-half dollars for state cases needing hospital care. The Incorrigible Consumptive bill was defeated but will probably be favorably reported upon by the Committee on Public Health to the present Legislature. Another bill which has been passed provides that all prisoners sentenced to more than thirty days' confinement must have at once a complete physical examination.

During the year 29 lectures on tuberculosis and industrial nursing have been given. The Boston Association has loaned to the league the educational film "The Great Truth." It was used in five Cambridge motion picture houses. Over 18.000 persons have viewed the "Health in Industry" exhibit. At one of the meetings of the executive committee war prohibition and the war program of the N. T. A. were endorsed. During 1917 there were about 5375 deaths from tuberculosis. Of these, 4600 were from pulmonary, and 775 from other forms of tuberculosis. There are over 3300 public and private beds for tuberculous patients in the State, of which 1065 are in state sanatoria; the new county hospitals, when completed, will greatly add to the facilities for treating patients who are at present a menace to their families while staying in their homes.—*Annual Report of the Massachusetts Anti-Tuberculosis League, 1918. E. M. Spofford, Boston M. and S. J., June 30, 1918, clxxviii, No. 25, 858.*

Remarks on Tuberculosis.—The activity of the State of Massachusetts in tuberculosis has been a distinct advantage to the general practitioner, as evinced by the replies received from numerous physicians on this subject. This state has a definite plan for anti-tuberculous work. Doctors in their private practice or in tuberculosis dispensaries, will be depended upon to make the diagnosis as early as possible. Favorable cases will be referred to the state sanatoria. In the large cities tuberculosis hospitals will continue to care for the advanced and the progressive cases, who cannot or should not leave home. The county tuberculosis hospitals will fill the gap now existing between the sanatorium and the local tuberculosis hospital. Emergency cases and all the patients from the scattered agricultural communities, and from the smaller towns and villages will be cared for in these county institutions, whence favorable cases will be transfered to the sanatoria.

The author has encountered two types of diagnostic mistakes committed by the general practitioner. First, patients in whose lungs the signs are vague, are assured by their physicians that they have no tuberculosis, in spite of the fact that constitutional symptoms are present, and probably of tuberculous nature. Second, patients with acute and subacute pulmonary infections, of pneumococcic or streptococcus origin, are diagnosed as tuberculous. In these the author urges that the history and symptoms are of more importance than the local pulmonary signs, and with proper care the correct diagnosis can be made.

Sanatorium treatment is preferable to the home treatment, especially when dealing with the poor and unintelligent. Tuberculin treatment and artificial pneumothorax should only be applied if the patient is under absolute supervision in a hospital or sanatorium. Heliotherapy has its greatest sphere of usefulness in non-pulmonary tuberculosis, particularly in bone and joint cases. However it may be used as an adjunct to the open air treatment in pulmonary tuberculosis. Out door sleeping and open air schools are to be encouraged, yet they should not be carried to extremes. Very cold weather is not beneficial and is often harmful. Rest is of great importance, and when indicated should be absolute i.e., the patient should avoid any unnecessary movements. Excessive cough should be stopped. X-ray is of great value in diagnosis, but should always be subsidiary to a careful physical examination.—*Random Remarks on Tuberculosis, J. B. Hawes, II, Boston M. & S. J., May 2, 1918, clxxviii, No. 18, 589.*

Framingham Sickness Census.—The Community Health Station at Framingham conducted a census of all the families in the town for the purpose of determining the number and variety of disease and minor conditions for comparison with those found at the end of the experiment. All sorts of ailments were included. The most common affections found were: colds, 13.5 per cent; heart disease, 8.6 per cent; rheumatism, 6.6 per cent; diseases of the stomach, 5.9' per cent; tuberculosis, 3.9 per cent; "cough," 3.9 per cent; bronchitis, 3.9 per cent; influenza, 2.7 per cent; nervousness, 2.7 per cent; diseases of the kidneys, 2.7 per cent. There were in all 407 diseased conditions. Of these, 77 were under fifteen years of age; 99 between fifteen and thirty-four; 120 between thirty-five and fifty-four; 99 over fifty-five; and 12 of unknown age. There was a rather high percentage in the advanced age period. There were 3212 individuals actually examined, of which 248 were among those recorded ill, a sickness per cent of 7.7. The group which refused examination totalling 3370, had a sickness rate of 4.70 per cent. Of the 16 presumably definite cases of pulmonary and non-pulmonary tuberculosis, 12 were finally examined. The sickness rate for the entire group, 6.2 per cent is a higher rate than has ever been recorded previously and compares with other localities as follows: North Carolina, 2.8 per cent; Boston, 1.9 per cent; Rochester, 2.1 per

cent. The higher rate is due to the more intensive publicity preceding the census and to the more liberal definition of sickness adopted for the study. According to a strict definition of disability as used in the Metropolitan Life Company surveys, the rate would be 1.8 per cent. The number of individuals per family was 4.52, which is higher than the average as it included lodgers and help residing with the family. The rate of disability as compared with that of other communities was: Framingham, 54.1 per cent; Boston, 91.9 per cent; Rochester, 82.8 per cent; and North Carolina, 80.4 per cent. The percentage of total illness receiving medical attention was also relatively high, 81.1 per cent as compared with Boston, 72.9; Rochester, 61; North Carolina, 61.5. While the sex distribution of individuals covered was almost equal the sickness incidence was rather high for the females, 70.4, as compared with 53.1 for males. However, the rate of sickness for females of all ages drops to 64.6 when pregnancies, miscarriages, childbirths and uterine disturbances are eliminated. The rates among the nationality groups were: English, 15.2; Canadian, 10.2; American, 8.4; Irish, 6.2; Italian, 4.9; Polish, 1.4. It is evident that the nationality groups showing the highest percentage of illness coincide with those groups best able to understand the queries presented to them. According to the classification by economic condition, and on a basis of 4.52 people per family (the figure of the census as a whole) the rate of illness 5.2 for those classed as in good economic condition; 7.4 for those in fair, poor and bad condition; and 5.2 for those whose economic condition was not given. There was even a smaller difference between families classed as "good" and those classed as "poor" when only serious and obvious illness was considered. There were 38 cases of suspicious and definite tuberculosis, of which 16 were finally classed as most probably tuberculous, a percentage of 0.24 of the whole group and 3.9 of the total illnesses. The rural sickness census showed a rate for the whole group of 10.4 per cent, 6.5 males and 14.4 females. A large percentage was found in the higher age groups. Of those unable to work there were 52.1 per cent, of which 36.8 per cent were up and about, only 47.4 had the attention of a physician as compared with 81.1 among the urban population.—*The Sickness Census. Framingham Monograph No. 2: Framingham Community Health and Tuberculosis Demonstration of the N. T. A., June, 1918.*

Illinois Plan for Tuberculosis Soldiers.—An agreement has been reached between the State Department of Health, the State Tuberculosis Association and the American Red Cross, according to which the Central Division of the Red Cross, through the Home Service Sections of its local chapters, will provide care to returned tuberculous soldiers in the interim between their return to their home communities and the time that more permanent provision is made for them, and shall also provide one-third of the expense for the more permanent care. An expert examination and diagnosis will be made by the Illinois Tuberculosis Association, and reports will be submitted to the State Department of Public Health so far as they may affect the control and prevention of communicable diseases. Under no circumstances will a tuberculous soldier be housed in a county almshouse, except when absolutely unavoidable. The remaining two-thirds of the cost of permanent cure are to be provided for by local organizations and individuals through the solicitation by the State Tuberculosis Association. The latter will also demand full reports of progress from physicians or institutions to whom the care of patients is intrusted.—*Medical Notes, Boston M. and S. J., clxxviii, No. 25, 882.*

Tuberculosis and War.—To meet the increase in tuberculosis which we have to expect in our civil population on account of the war, we must depend upon wise legislation and philanthropy. The practical question to-day for us is the exclusion from the army of active or quiescent cases of tuberculosis. Regarding the question of how much of quiescent trouble is still compatible with army work, the author takes the view of Maragliano that no man who has any active or latent lesion in the lungs should be admitted to the army. Any subject, showing fairly extensive shadows upon examination with the x-ray, and which an expert recognizes as being of tuberculous nature, is unfit for service. Thickening of the glands around the roots of the lungs, however, can be overlooked. Soldiers who contract the disease while in the service and are returned should never be allowed to remain with their families, but should be treated in special sanatoria. Preparations should be made for a terrible increase in the incidence and mortality of tuberculosis after the war.—*The War in Its Effects upon the Development of Tuberculosis, C. L Minor, South, M. J., January, 1918; xl, No. 1, 25.*

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* "The Choice of Tuberculins," by Benjamin White, Otisville, N. Y., Department of Health, City of New York. Read at the annual meeting of the Medical Society of the State of New York, at Saratoga Springs, May 18, 1916.

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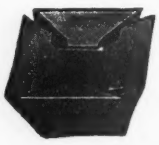

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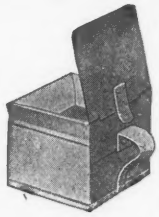

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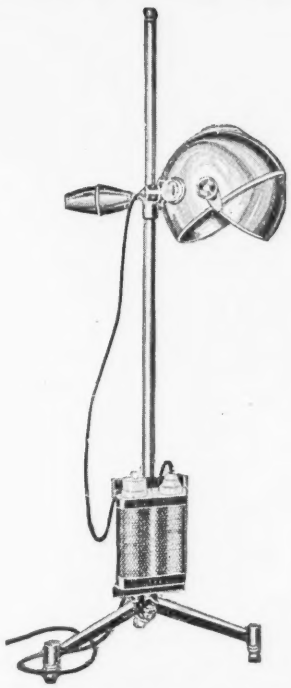

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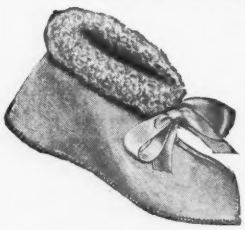

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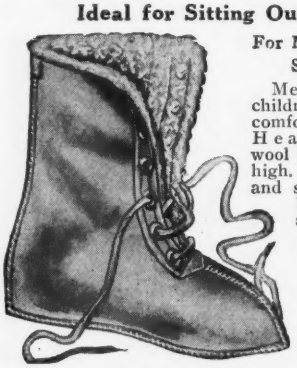

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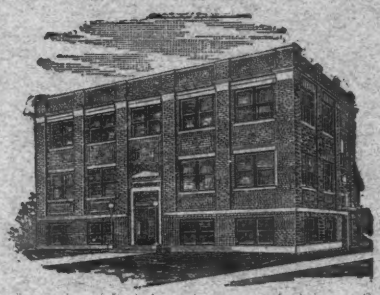

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